International Conference on Biomedical Application of Nanomaterials

Program & Abstracts Book

2-5 December 2015
City University of Hong Kong
Hong Kong

Organisers:

超金剛石及
先進薄膜研究中心
Center Of Super-Diamond
and Advanced Films

物理及材料科學系
Department of Physics
and Materials Science

CityU
香港城市大學
City University of Hong Kong

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K.C. WONG EDUCATION FOUNDATION

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ICOBAN2015

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City University of Hong Kong, Hong Kong

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LI, Quan, The Chinese University of Hong Kong
LI, Yangyang, City University of Hong Kong
LU, Yang, City University of Hong Kong
SHI, Peng, City University of Hong Kong
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YU, Denis Y.W., City University of Hong Kong
ZAPIEN, Antonio, City University of Hong Kong
ZHENG, Zijian, Hong Kong Polytechnic University

SPONSOR:

The organizers gratefully acknowledge financial support from:-

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PLENARY* & INVITED SPEAKERS: (IN ALPHABETICAL ORDER)

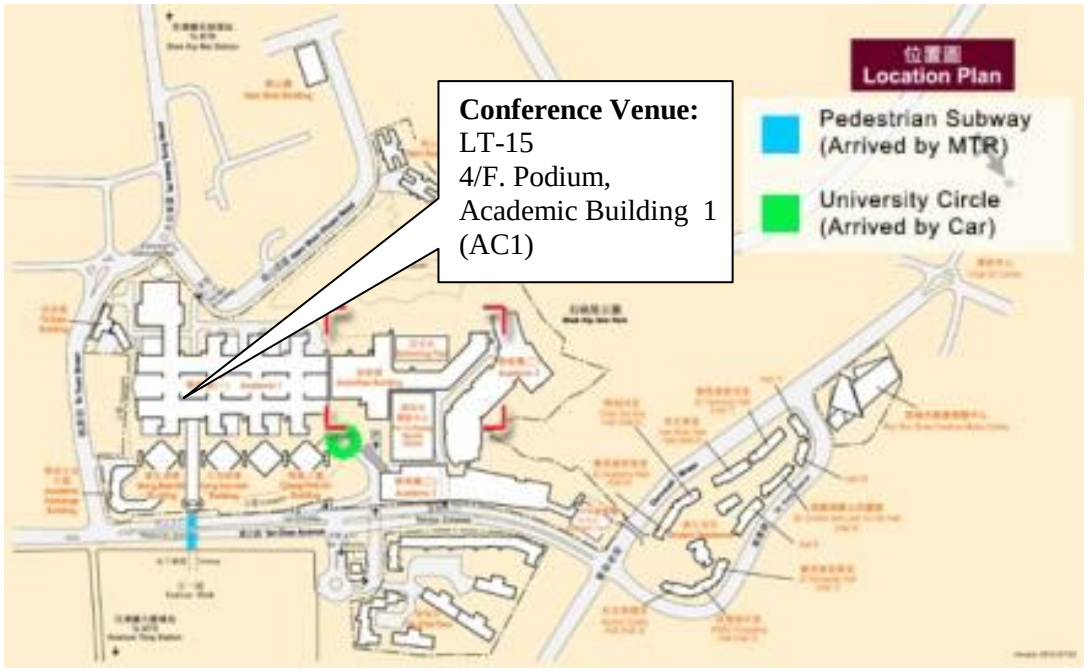
CHANG, Chia-Ching, *National ChiaoTung University, Taiwan*
CHEN, Peng, *Nanyang Technological University, Singapore*
CHEN, Xueyuan, *Fujian Institute of Research on the Structure of Matter, CAS, China*
CHENG, Shuk Han, *City University of Hong Kong, Hong Kong*
GAO, Mingyuan, *Institute of Chemistry, CAS, China*
HE, Mingliang, *City University of Hong Kong, Hong Kong*
HO, Rodney J.Y., *University of Washington, U.S.A.*
HOU, Yanglong, *Peking University, china*
****HYEON, Taeghwan,*** *Seoul National University, Korea*
IMAHORI, Hiroshi, *Kyoto University, Japan*
JIANG, Xingyu, *National Center for Nanoscience and Technology of China, China*
KIM, Won Jong, *Pohang University of Science and Technology, Korea*
LAN, Hui-Yao, *The Chinese University of Hong Kong, Hong Kong*
LI, Quan, *The Chinese University of Hong Kong, Hong Kong*
LIANG, Xing-Jie, *National Center for Nanoscience and Technology of China, China*
LIU, Zhuang, *Soochow University, China*
LIU, Gang, *Xiamen University, China*
LIU, Bin, *National University of Singapore, Singapore*
****LOVELL, Jonathan F.,*** *University at Buffalo, USA*
NOH, Insup, *Seoul National University of Science and Technology, Korea*
PANG, Daiwen, *Wuhan University, China*
****SAILOR, Michael J.,*** *University of California, San Diego, USA*
SHEN, Youqing, *Zhejiang University, China*
SHI, Xiangyang, *Donghua University, China*
SHI, Peng, *City University of Hong Kong, Hong Kong*
****SHI, Jianlin,*** *Shanghai Institute of Ceramics, CAS, China*
SUNG, Hsing-Wen, *National Tsing Hua University, Taiwan*
TANG, Zhiyong, *National Center for Nanoscience and Technology of China, China*
TANG, Benzhong, *Hong Kong University of Science and Technology, Hong Kong*
WANG, Shutao, *Technical Institute of Physics and Chemistry, China*
WANG, Hua, *Henan University, China*
WANG, Pengfei, *Technical Institute of Physics and Chemistry, China*
XU, Qinghua, *National University of Singapore, Singapore*
XU, Guangchen, *Wiley, China*
YANG, Michael Mengsu, *City University of Hong Kong, Hong Kong*
ZHANG, Xiaohong, *Soochow University, China*

CONFERENCE INFORMATION

Venue	*Lecture Theatre 15*, 4/F. Podium, Academic Building 1, City University of Hong Kong
Phone No.	+852 3442 4204
Fax. No.	+852 3442 0541
Mailing Address	Center Of Super-Diamond and Advanced Films (COSDAF), & Department of Physics and Materials Science City University of Hong Kong Tat Chee Avenue, Kowloon Tong Hong Kong SAR
E-mail	ICOBAN2015@cityu.edu.hk / apcosdaf@cityu.edu.hk
Website	http://www.cityu.edu.hk/cosdaf/ICOBAN2015/Index.html

CONFERENCE VENUE DIRECTION:

Venue: **Lecture Theatre 15**
4/F. Podium, Academic Building 1,
City University of Hong Kong



City University is located near the Kowloon-Tong Mass Transit Railway (MTR) station and can be easily accessed via the #3M entrance of the Academic Building by the following transportation means:

- MTR
- Taxis

Arrived at Pedestrian Subway

1. Take MTR East Rail Line or MTR Kwun Tong Line to "Kowloon Tong" station.
2. Exit at "Festival Walk" Exit C2
3. Find **Shop LG1-10,** take the escalator next to it, which bring you to a **pedestrian subway** leading to CityU.
4. Pass through the pedestrian subway, go straight, and enter Academic 1.
5. Turn right and take the escalator to level 4 to the Podium
6. You will find the Signage to Lecture Theatre 15.

Arrived at University Circle (U-Circle)

1. When you drop off at the University Circle, go along the covered walkway which will lead you to the Academic Building 1.
2. Walk through the red doors, you will be on the 4th floor of Academic Building 1.

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DETAILS OF TECHNICAL PROGRAM

WEDNESDAY
December 2, 2015

16:00 – 19:00 **Registration** *with Welcoming Reception*
[Venue: LT-15, Academic Building 1]

THURSDAY
December 3, 2015

07:45 **Registration**
[Venue: LT-15, Academic Building 1]

08:45 **Welcome & Opening**
[Venue: LT-15, Academic Building 1]
LEE Chun-Sing
City University of Hong Kong, Hong Kong

Session I – Synthesis and Assembly of Nanomaterials for Biomedical Applications I

Venue: LT-15, Academic Building 1
Chairman: LOVELL, Jonathan F.(University at Buffalo, USA)

09:00 1.1 **Designed Chemical Synthesis and Assembly of Uniform-sized Nanoparticles for Medical Applications**
HYEON Taeghwan,
Seoul National University, Korea [Plenary]

09:45 1.2 **Hydrophobic/Amphiphilic drug delivery system development by reconstituted apolipoprotein B lipoparticle**
CHANG Chia-Ching, CHU Hsueh-Liang, CHEN Gong-Shen
National Chiao Tung University, Taiwan [Invited]

10:10 1.3 **The Design and Synthesis of Helix, Double Helix Shaped Molecules**
LI Chunli, ZHANG Sheng, SONG Jinsheng, LIU Xinming, WANG Hua
Henan University, China [Invited]

10:35 BREAK & POSTER VIEWING

Session II – Synthesis and Assembly of Nanomaterials for Biomedical Applications II

Venue: LT-15, Academic Building 1

Chairman: HYEON Taeghwan (Seoul National University, Korea)

10:50	2.1	**Stimuli-Responsive Nanoparticles for Gene, Drug Delivery and Nitric Oxide Delivery** *KIM Won Jong*, University of Science and Technology (POSTECH), Korea [Invited]
11:15	2.2	**Graphene Quantum Dots for Biomedical Applications** *CHEN Peng*, Nanyang Technological University, Singapore [Invited]
11:40	2.3	**AIE Dots for Biosensing, Imaging, Diagnosis and Therapy** *TANG Benzhong*, The Hong Kong University of Science & Technology, Hong Kong[Invited]
12:05	2.4	**Fabrication of CdTe quantum dots coated SiO2 and its application in photoluminescence immunosensor** *YAN Mei, CHU Chengchao* University of Jinan, China
12:20	2.5	**Catalytic applications of PtPd@CeO2 multicore@shell nanomaterials for the detection of cancer antigen 153** *ZHANG Lina, YU Jinghua* University of Jinan, China

12:35	GROUP PHOTO TAKING

12:50	LUNCH *(City Top Restaurant, 9/F, Amenities Building)*

Session III – Nanomaterials for Diagnostic and Bioimaging I

Venue: LT-15, Academic Building 1

Chairman: SUNG Hsing-Wen (National Tsing Hua University, Taiwan)

14:00	3.1	**Therapeutic and Diagnostic Nanoparticles Based on Porous Silicon** *SAILOR Michael J.* University of California, San Diego, USA [Plenary]
14:45	3.2	**Functional Nanoparticles for Tumor Imaging** *HOU Yi, LIU Chunyan, QIAO Ruirui, GAO Zhenyu, GAO Mingyuan*, Institute of Chemistry, CAS, China [Invited]
15:10	3.3	**Lanthanide-Doped Luminescent Nano-Bioprobes for In Vitro Detection of Tumor markers** *CHEN Xueyuan* Fujian Institute of Research on the Structure of Matter, CAS, China [Invited]

15:35	BREAK & POSTER VIEWING

Session IV – Nanomaterials for Drug Delivery and Tissue Engineering

Venue: LT-15, Academic Building 1

Chairman: SAILOR Michael J. (University of California, San Diego, USA)

15:55	4.1	**Bubble-Generating Carrier Systems for Localized Controlled Release** *CHEN Ko-Jie, CHUNG Ming-Fan, HSIAO Chun-Wen, LIAO Zi-Xian, CHIA Wei-Tso, LIN Kun-Ju, SUNG Hsing-Wen* National Tsing Hua University, Taiwan [Invited]
16:20	4.2	**Effects of Nano/Micro-Patterned Hydrogels and Nano/Micro Gel Particles on Bone Tissue Engineering** *Sumi BANG, Dian Purwita SARIL, LeTuyen NGUYEN, Insup NOH* Seoul National University of Science and Technology, Korea [Invited]
16:45	4.3	**The use of folate-PEG-grafted-hybranched-PEI nonviral vector for the inhibition of glioma growth in the rat** *HE Mingliang* City University of Hong Kong, Hong Kong [Invited]
17:10	4.4	**Nano-functionalized Silk for Smart Wearable Devices** *LU Zhisong, MENG Mei, MAO Cuiping, XIAO Jing, ZHANG Huihui* Southwest University, China
17:25	4.5	**Publishing in Wiley Materials Science Journals** *XU Guangchen* Deputy editor of Small, Advanced Energy Materials and Advanced Science, China [Invited]

17:50	BANQUET

FRIDAY
December 4, 2015

Session V – Synthesis and Assembly of Nanomaterials for Drug Delivery

Venue: LT-15, Academic Building 1

Chairman: SHEN Youqing (Zhejiang University, China)

09:00	5.1	**Mesoporous silica nanoparticles: controlled synthesis and biomedical applications** *SHI Jianlin* Shanghai Institute of Ceramics, CAS, China [Plenary]
09:45	5.2	**Microfluidic-based Approaches for Controllable Synthesis of Nanoparticles** *SUN Jiashu, FENG Qiang, ZHANG Lu, JIANG Xingyu* National Center for NanoScience and Technology (NCNST), China [Invited]
10:10	5.3	**Systems Approach to Transform Nanomaterials to Nanomedicines From Concept to Practice with Nanodrugs for AIDS and Cancer** *HO Rodney J.Y.* University of Washington, Seattle, USA [Invited]
10:35	5.4	**Targeting gene therapy for tissue fibrosis using an ultrasound-microbubble technique** *LAN Hui-Yao* The Chinese University of Hong Kong, Hong Kong [Invited]
11:00	5.5	**Functionalized boron nitride nanosphere as carrier for enhancing the immunostimulatory effect of CpG oligodeoxynucleotide** *ZHANG Huijie, ZHI Chunyi, GAO Xiao-dong, HANAGATA Nobutaka* Jiangnan University, China

11:15 BREAK & POSTER VIEWING

Session VI – Nanomaterials for Cancer Theranostics I

Venue: LT-15, Academic Building 1

Chairman: JIANG Xingyu

(National Center for NanoScience and Technology (NCNST), China)

11:35	6.1	**Stimuli-regulated Cancer Theranostics Based on Magnetic Nanoparticles** *HOU Yanglong* Peking University, China [Invited]
12:00	6.2	**Subcellular Behaviors Evaluation of Nanopharmaceuticals with Aggregation-Induced Emission Molecules** *XUE Xiangdong, XU Jing, WANG Paul C, LIANG Xing-Jie* National Center for Nanoscience and Technology, China [Invited]
12:25	6.3	**Novel nano-theranostics based on human serum albumin** *LIU Zhuang* Soochow University, China [Invited]

12:50 LUNCH *(City Top Restaurant, 9/F, Amenities Building)*

Session VII – Nanomaterials for Phototherapies

Venue: LT-15, Academic Building 1

Chairman: LIANG Xing-Jie
(National Center for Nanoscience and Technology, China)

13:55 7.1 **Self-assembled Porphyrins for Applications in Imaging and Drug Delivery**
LOVELL Jonathan F.
University at Buffalo, USA [Plenary]

14:40 7.2 **Carbon Dots for Photodynamic and Photothermal Therapy**
LIU Weimin, GE Jiechao, WANG Pengfei
Technical Institute of Physics and Chemistry, CAS, China [Invited]

15:05 7.3 **AIE Probes for Biomedical Applications**
LIU B., Ding D., LI K., LIANG J, TANG B. Z.
National University of Singapore, Singapore [Invited]

15:30 7.4 **Molecular Engineering of Photofunctional Materials for Biological Applications**
Hiroshi IMAHORI
Kyoto University, Japan [Invited]

15:55 7.5 **Effects of gold nanorods on eliminating the amyloid-β aggregates with laser irradiation**
LIN D. D., HE R.Y., LI P., YANG X. J.
Fudan University, China

16:10 POSTER SESSION

Session VIII – Nanomaterials for Bio-Detection and Sensing

Venue: LT-15, Academic Building 1

Chairman: SHI Jianlin (Shanghai Institute of Ceramics, CAS, China)

17:10 8.1 **Targeted Destruction of Cancer Stem Cells by Nanomedicine**
LIU Dandan, WANG Weimao, FONG Chi-Chun, YIP Timothy T. C., AU Joseph S. K., YANG Mengsu (Michael)
City University of Hong Kong, Hong Kong [Invited]

17:35 8.2 **A simple and sensitive fluorescence method for activity analysis and effects screen in vitro and vivo of Mung Bean Nuclease based on graphene oxide**
PENG Lan, XIE Zhenhua,TONG Chunyi, LIU Xuanming, LIU Bin*
Hunan University, China

17:50 8.3 **Rapid, Multiplexed, Mobile Phone-Enabled Point of Care Diagnostic Device to Detect Infectious Diseases**
YEN Chun-Wan, Helena de PUIG, TAM Justina, Kimberly HAMAD-SCHIFFERLI, LEE Gehrke
Massachusetts Institute of Technology, USA

18:05 8.4 **2D and 3D Surface Enhanced Raman Scattering (SERS) Substrate for Real Application**
HUANG Longbiao, VELLAISAMY Roy
Northwestern Polytechnical University, China

SATURDAY
December 5, 2015

Session IX – Nanomaterials for Diagnostic and Bioimaging II

Venue: LT-15, Academic Building 1

Chairman: IMAHORI Hiroshi (Kyoto University, Japan)

09:00 9.1 **Engineering biointerface with controlled cell adhesion towards cancer diagnostics**
WANG Shutao
Technical Institute of Physics and Chemistry, CAS, China [Invited]

09:25 9.2 **High Luminescent Organic Dye Nanoparticles for Bioimaging**
ZHANG Xiujuan, ZHANG Xiaohong
Soochow University, China [Invited]

09:50 9.3 **Conjugation of Ultrasmall Iron Oxide Nanoparticles onto Multifunctional Dendrimers for SPECT/MR Dual-Mode Imaging of Gliomas**
LUO Yu, ZHAO Lingzhou, XIONG Zhijuan, ZHAO Jinhua, SHI Xiangyang
Donghua University, China [Invited]

10:15 BREAK & POSTER VIEWING

Session X – Nanomaterials for Cance Theranostics II

Venue: LT-15, Academic Building 1

Chairman: WANG Shutao
(Technical Institute of Physics and Chemistry, CAS, China)

10:35 10.1 **Virus-Mimetic Nanovesicles as a Versatile Antigen Delivery System**
ZHANG Pengfei, LIU Gang
Xiamen University, CAS, China [Invited]

11:00 10.2 **Anti-cancer Nanotherapeutics: smart delivery, efficacy and toxicity**
CHENG Shuk Han
City University of Hong Kong, Hong Kong [Invited]

11:25 10.3 **Surface Ligand in Modification and Assembly of Multifunctional Nanoparticles for Biomedical Applications**
LING Daishun

11:40 10.4
Zhejiang University, China **Interfacial assembly and theranostic applications of organic-inorganic hybrid nanomaterials**
LEUNG Cham-Fai Ken
The Hong Kong Baptist University, Hong Kong

11:55 LUNCH *(City Top Restaurant, 9/F, Amenities Building)*

Session XI – Interaction of Nanomaterials with Cells

Venue: LT-15, Academic Building 1

Chairman: KIM Won Jong

(University of Science and Technology (POSTECH), Korea)

13:15 11.1 **Design of 3S Transition-Nanocarriers for Cancer Drug Delivery Cascade**

SHEN Youqing

Zhejiang University, China [Invited]

13:40 11.2 **Tracking single viruses infecting their host cells using quantum dots**

LIU Shu-Lin, ZHANG Zhi-Ling, PANG Dai-Wen

Wuhan University, China [Invited]

14:05 11.3 **Diamond Nanointerface for Signal Dissection in Live Neuronal Cells**

SHI Peng

City University of Hong Kong, Hong Kong [Invited]

14:30 11.4 **Interaction of Nanodiamond with Cells: characteristics, implication, and applications**

CHU Zhiqin, ZHANG BoKai, FENG Xi, WANG Yanhuang, CHANG Huancheng, WRACHTRUP Joerg, LIN Ge, CIGLER Petr, LIU Renbao, LI Quan

The Chinese University of Hong Kong, Hong Kong [Invited]

14:55 11.5 **The effect of carbon nanotubes on the aggregation of amyloid-β peptides**

LIN D. D., MA Q. Q., YANG X. J.

Fudan University, China

15:10 BREAK & POSTER VIEWING

Session XII – Nanomaterials for Diagnostic and Bioimaging II

Venue: LT-15, Academic Building 1

Chairman: PANG Dai-Wen (Wuhan University, China)

15:25 12.1 **Core-Shell Upconversion Nanoparticle@Metal-Organic Framework Nanoprobes for Luminescent/Magnetic Dual-mode Targeted Imaging**

LI Yantao, TANG Jinglong, LIU Yaling, CHEN Chunyin, TANG Zhiyong

National Center for Nanoscience and Technology, China [Invited]

15:50 12.2 **Nanomaterials for Two-photon Imaging and Phototherapy**

XU Qing-Hua

National University of Singapore, Singapore [Invited]

16:15 12.3 **Highly sensitive colorimetric detection of protein O-GlcNAcylation based on gold nanopartilce-catalyzed signal amplification**

LIU Yingshuai, XIE Jin, YU Jie

Southwest University, China

16:30 12.4 **Circularly polarized photocatalytic activity in gold-nanogap-silver chiroplasmonic nanoparticles**

XU Liguang, WU Xiaoling, MA Wei, WANG Libing, KUANG Hua, XU Chuanlai

Jiangnan University, China

17:00 CLOSING REMARKS & BEST POSTER AWARD PRESENTATION

----- End -----

FRIDAY
December 4, 2015

Poster Session

Venue: Outside LT-15, Academic Building 1
Time: 15:55-16:55

P-01 **A carrier-free strategy to fabricate nanoparticles for chemo-photodynamic synergistic therapy**
DENG, Xin, LIANG Yan, SU Ting, PENG Xinyu, CAO Jun, HE Bin, GU Zhongwei
Sichuan University, China

P-02 **Ag/Si nanowire array embedded microfluidic chips: an in-situ surface enhanced Raman spectroscopy monitoring platform**
ZHAO, Yingqi, ZHANG Yong-Lai, CHEN Xianfeng, ZHANG Wenjun
City University of Hong Kong, Hong Kong

P-03 **Protective Autophagy in AgNPs Associated Radiotherapy for Glioma**
WU, Hao, LIN Jun, LIU Peidang, HUANG Zhihai, WANG Cailian, WEN Longping, GU Ning
Southeast University, China

P-04 **Layered Double Hydroxide Nanoparticles for Drug Delivery and Bioimaging**
YAN, Li, ZHU Xiaoyue, CHEN Xianfeng, ZHANG Wenjun
City University of Hong Kong, Hong Kong

P-05 **Terminal moieties effects on the drug delivery properties of PEG-PCL polymeric micelles**
LIANG, Yan, DENG Xin, ZHANG Longgui, HE Bin
Sichuan University, China

P-06 **Self-Monitoring and Self-Delivery of Photosensitizer-Doped Nanoparticles for Highly Effective Combination Cancer Therapy in Vitro and in Vivo**
ZHANG, Jinfeng, CHANG Chia-Ching, ZHANG Xiaohong, LEE Chun-Sing
City University of Hong Kong, Hong Kong

P-07 **Preparation and Preliminary Application of Magnetic Nanocrystal/Polymer Composite Beads**
NIU Mu, DU Meihong, GAO, Zhenyu, YANG Chunhui, LU Xianyong, QIAO Ruirui, GAO Mingyuan
Institute of Chemistry, CAS, China

P-08 **Amphiphilic dendrimer delivering BCL-3 siRNA for potent nasopharyngeal carcinoma therapy**
MA, Jing, WONG Alice ST
The University of Hong Kong, Hong Kong

P-09 **Magnetic materials based electrochemiluminescence immunoassay using home-made detecting cell**
ZHANG, Yan, GE Shenguang, YU Jinghua
University of Jinan, China

P-10 **Self-carried curcumin nanoparticles for in vitro and in vivo cancer therapy with real-time monitoring of drug release**

LI, Shengliang, ZHANG Jinfeng, ZHANG Xiaohong, LEE Chun-Sing, JIANG Xing-Jie

National Center for Nanoscience and Technology of China, China

P-11 **Ultrasensitive electrochemiluminescence sensor for detection of mercury ion on portable paper-based device**

YU, Jinghua, ZHANG Yan, GE Shenguang

University of Jinan, China

P-12 **Synthesis of slilica g-C3N4 nanodots gels toward White-Light-Emitting Devices**

WANG, Aiwu, LU Jian, LI Yang Yang

City University of Hong Kong, Hong Kong

P-13 **The Biological Application of Rare Earth Upconversion Luminescence Nanoparticles**

LIU, Chunyan, HOU Yi, HUANG Jiayi, QIAO Ruirui, GAO Mingyuan

Institute of Chemistry, CAS, China

P-14 **Carbon dot-based fluorescence turn-on sensor for hydrogen peroxide with a photo-induced electron transfer mechanism**

LAN, Minhuan, DI Yanfei, ZHANG Wenjun

City University of Hong Kong, Hong Kong

P-15 **A pH-sensitive micelle based on poly(ethylene glycol)-b-poly(L-lysine) copolymer for anticancer drug delivery**

ZHANG, Longgui, LI Junhua, HE Bin

Sichuan University, China

P-16 **Graphitic Carbon Nitride Nanosheet @ Metal-Organic Framework Core-shell Nanoparticles for Photo-chemo Combination Therapy**

CHEN, Rui, ZHANG Jinfeng, LEE Chun-Sing

City University of Hong Kong, Hong Kong

P-17 **A pH-Controlled Nitric Oxide-Generating Hollow Microsphere System for Overcoming P-Glycoprotein-Mediated Multidrug Resistance for Cancer Therapy**

LIN, Yu-Jung, CHUNG Ming-Fan, LIU Hung-Yi, LIN Kun-Ju, CHIA Wei-Tso, SUNG Hsing-Wen

National Tsing Hua University, Taiwan

P-18 **Flow Synthesis of Biocompatible Fe3O4 Nanoparticles: Insight into the Effects of Residence Time, Fluid Velocity, and Tube Reactor Dimension on Particle Size Distribution**

JIAO, Mingxai, ZENG Jianfeng, JING Lihong, LIU Chunyan, GAO Mingyuan

Institute of Chemistry, CAS, China

P-19 **Multifunctional magnetic hydrogel with controllable magnetothermal effect in alternating magnetic field**

HU, Ke, SUN Jianfei, GUO Zhaobin, WANG Peng, MA Siyu, MA Ming, ZHANG Tianzhu, GU Ning

Southeast University, China

P-20 **Interrogation of Cellular Innate Immunity by Diamond-NanoneedleAssisted Intracellular Molecular Fishing**

WANG, Zixun, YANG Yang, XU Zhen, WANG Ying, ZHANG Wenjun, SHI Peng

City University of Hong Kong, Hong Kong

P-21 **A Protease-activated Ratiometric Fluorescent Probe for pH-mapping of Malignant Tumor**

HOU, Yi, ZHOU Jin, GAO Zhenyu, SUN Xiaoyu, LIU Chunyan, SHANGGUAN Dihua, YANG Wensheng, GAO Mingyuan

Institute of Chemistry, CAS, China

P-22 **Flexible and Highly Reproducible Printed Surface Enhanced Raman Spectroscopy Substrates for the Detection of Chemicals and Drugs**

WU, Wei, VELLAISAMY A.L. Roy

City University of Hong Kong, Hong Kong

P-23 **Low-Cost Graphene Quantum Dots with Peroxidase Catalytic Activity**

HAN, Yanwei, ZENG Yan, ZHOU Ying, LIU Yuchen, LIANG Feng

Wuhan University of Science and Technology Wuhan, China

P-24 **Diamond nanoneedle arrays for enhanced delivery of drug molecules to different cell lines**

ZHU, Xiaoyue, CHEN Xianfeng, ZHANG Wenjun

City University of Hong Kong, Hong Kong

P-25 **Investigation of biological cell–small molecular interactions based on gold film SPR sensor using a LSCI–SPR**

ZHANG Hongyan, LIU Weimin, LIU Sha, GE Jiechao, WU Jiasheng WANG Pengfei

Technical Institute of Physics and Chemistry, CAS, China

P-26 **One-Step Reaction for Fluorescent Silicon Nanorods**

GE Jiechao, JIA Qingyan, LIU Weimin, ZHANG Hongyan, WANG Pengfei

Technical Institute of Physics and Chemistry, CAS, China

P-27 **Mono-disperse Silver Quantum Dots Modified Formvar Films**

LI Fu-Qiang, LI Chun-Sing, MENG Xiang-Ming

Technical Institute of Physics and Chemistry, CAS, China

----- End -----

Abstract of Talks

Designed Chemical Synthesis and Assembly of Uniform-sized Nanoparticles for Medical and Energy Applications

Taeghwan Hyeon*

Center for Nanoparticle Research, Institute for Basic Science (IBS), Seoul 151-742, Korea, and School of Chemical and Biological Engineering, Seoul National University, Seoul 151-742, Republic of Korea. E-mail: thyeon@snu.ac.kr

Over the last 10 years, our laboratory has focused on the designed chemical synthesis, assembly and applications of uniform-sized nanocrystals. In particular, we developed a novel generalized procedure called as the "heat-up process" for the direct synthesis of uniform-sized nanocrystals of many metals, oxides, and chalcogenides.[1]

Recently our group has been focused on medical applications of various uniform-sized nanoparticles. Using 3 nm-sized iron oxide nanoparticles, new non-toxic MRI contrast agent was realized for high resolution MRI of blood vessels down to 0.2 mm.[2] We reported the first successful demonstration of high-resolution in vivo three-photon imaging using biocompatible and bright Mn^{2+} doped ZnS nanocrystals.[3] We fabricated tumor pH-sensitive magnetic nanogrenades composed of self-assembled iron oxide nanoparticles and pH-responsive ligands for theranostic application, enabling the visualization of small tumors of < 3 mm via pH-responsive T1 MRI and fluorescence imaging and superior photodynamic therapeutic efficacy in highly drug-resistant heterogeneous tumors.[4] We synthesized tumor pH-sensitive nanoformulated triptolide coated with folate targeting ligand to treat hepatocellular carcinoma (HCC), which has one of the worst prognosis for survival as it is poorly responsive to both conventional chemotherapy and mechanism directed therapy.[5]

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5. "pH-Sensitive Nanoformulated Triptolide as a Targeted Therapeutic Strategy for Hepatocellular Carcinoma," *ACS Nano* **2014**, 8, 8027.

1.2

Hydrophobic/Amphiphilic drug delivery system development by reconstituted apolipoprotein B lipoparticle

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Keywords: Drug delivery system, Apolipoprotein B, low density lipoprotein receptor, MRI image contrast reagent, Hsp90

It is challenging tasks to deliver hydrophobic and/or amphiphilic anticancer drug to the target tumor or to pass through the blood-brain barrier, without specific modification. Low-density lipoprotein (LDL) has been recognized as hydrophobic and/or amphiphilic transporter in human circulating system. Meanwhile, the LDL receptors are highly expressed in tumors and LDL can pass through the blood-brain barrier naturally. Therefore, LDL like drug delivery system is highly desirable. However, to reconstitute LDL with full length apolipoprotein B (apo B) is infeasible until our research team reconstituting apoB lipoparticle (rABL) though the modified over-critical process in 2013. Our rABL exhibited good biocompatibility, which almost identical to native LDL, and enhanced the efficacy of anti-cancer therapy in model cells when the rABL loaded with anticancer drugs. Furthermore, rABL also exhibit the potential application as a MRI contrast agent carrier.

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The design and synthesis of helix, double helix shaped molecules

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Keywords: thiophene; helicene; double helix; synthesis; X-ray structure

The helical framework is one of amazing molecular structures in organic and bioorganic chemistry, and the construction of helical compounds shows very high challenge in organic synthesis. The thiophene oligmers are of current interests in organic optoelectronic materials and devices. In our work, two types of thiophene-based helices have been constructed. One is thiophene-based helicene based on dithienothiophene (**DTT**) as building blocks (Figure 1). The helicenes have been synthesized by thermal and photochemical methods. The helical structures are confirmed by X-ray analysis. Another one is thiophene-based double helix based on cyclooctatetrathiophene (**COTh**) as building blocks. A longest double helix with up to five tetraarylenes has been obtained (Figure 2). The X-ray crystallographic studies of four double helices unambiguously revealed that each double helical scaffold has two single helices intertwined with each other via the C-C single bonds. In addition, two double helicene-like compounds bridged by silicon have also been designed and synthesized (Figure 3). Their molecular structures are confirmed by X-ray analysis.

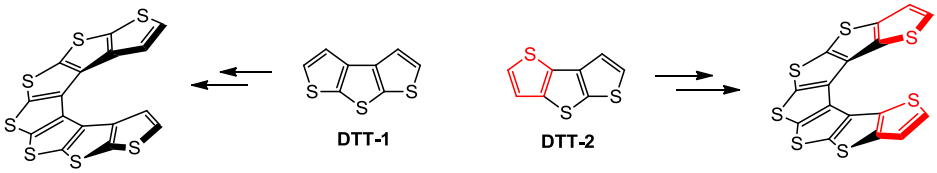

Figure 1. The structures of helicenes based on **DTT**

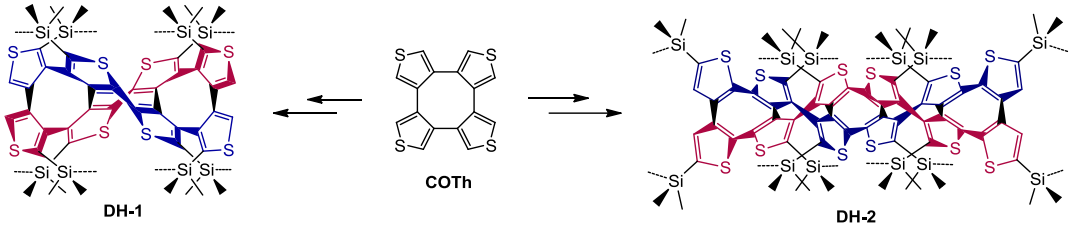

Figure 2. The structures of double helices based on **COTh**

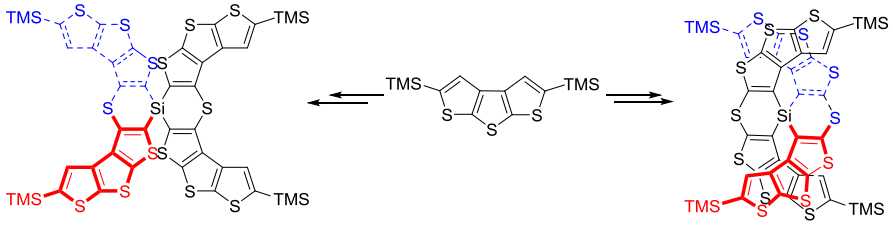

Figure 3. The structures of double helicene-like molecules based on **DTT-1**

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2.1

Stimuli-Responsive Nanoparticles for Gene, Drug Delivery and Nitric Oxide Delivery

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Keywords: Photothermal; i-motif; pH-responsive; Cyclodextrin; Nitric Oxide

For the synergistic gene therapy, gold nanoparticles were employed as photothermal agents or the templates for drug loading. The pH-responsive i-motif DNA was utilized for the effective intracellular performance of photothermal therapy and chemotherapy. The developed systems exhibited synergistic anticancer effects via combination of siRNA and photothermal/chemo therapy. In addition to gene delivery systems, self-assembled nanoparticles via multivalent host-guest chemistry between PTX and β-cyclodextrin (β-CD) were reported as a novel paclitaxel (PTX) delivery platform. CD and PTX were polymerized into the pCD and pPTX which provide the chance to produce the stable inclusion complex in blood circulation and release drug in intracellular regions. Furthermore, we also developed novel nitric oxide (NO) delivery system using catecholamine and diazeniumdiolates. Simple two-step reactions comprising catecholamine and diazeniumdiolates enable virtually any material surfaces to release NO with appreciable storage.

In the case of photothermal gene therapy, the i-motif DNA formed interstrand tetraplex in endosomal acidic pH, which could induce the formation of Au nanoclusters, resulting in endosomal escape of AuNP clusters and release of siRNA in the cytosol. As a result, when irradiated with laser, the synergistic anticancer effects was established by combination of photothermal ablation and gene silencing. For the synergistic gene and chemotherapy, the pH-responsive i-motif DNA facilitated the disassembly of the gold nanoclusters and dehybridization of i-motif/RNAi duplex, resulting in the release of therapeutic antisense RNA and Dox. Therefore, drug-mediated apoptosis was significantly accelerated by sensitizing the cancer cells to the drug. For the PTX delivery, the nano-assembly showed the high stability in blood and intracellular esterase-responsive drug release properties owing to the strong multivalent host-guest interactions and the ester bond linkages. This well-designed polymeric nano-carrier demonstrated a long-term suppression of tumor growth in vivo. Finally, in the case of surface NO delivery, the developed methods could offer a versatile platform which could be applied to surfaces of various materials and resulting surfaces could efficiently inhibit the bacterial adhesion, and kill adhered bacteria cells and yet demonstrate excellent biocompatibility.

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Graphene Quantum Dots for Biomedical Applications

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Due to the intrinsic limitations suffered by the current fluorophores (e.g., fluorescent proteins, organic dyes, and semiconductor quantum dots), seeking complementary or better fluorescent reporters is a constantly ongoing effort critical for the areas of bioimaging, optical sensing, photovoltaics etc. Graphene quantum dots (GQDs) are emerging as a new class of fluorophores with unique combination of several key merits including widely tunable photoluminescence properties, excellent photo- and chemical- stability, molecular size, and biocompatibility. GQDs promise a wide range of novel applications in biomedicine, energy storage and conversion, catalysis, etc. In this presentation, we demonstrate the methods to synthesize GQDs and the applications of these GQDs for real-time molecular imaging in live cells, ultrasensitive fluorescence detection of biomolecules, drug delivery, and electrochemical sensing of heavy metal ions.

2.3

AIE Dots for Biosensing, Imaging, Diagnosis and Therapy

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Keywords: aggregation-induced emission, nanoparticles, bio-application

Traditional π-conjugated fluorophors are prone to aggregate with light emission quenching which is known as aggregation-caused quenching (ACQ). We have observed an opposite phenomenon termed "aggregation-induced emission" (AIE) and identified the restriction of intramolecular rotation (RIR) as the main reason for the AIE effect. Guided by the RIR mechanism, we have developed a series of new AIE luminogens with emission colors covering the whole visible spectrum, fluorescence quantum yields up to unity. Nanoparticles of the AIE luminogens (alias "AIE dots") with efficient fluorescence and excellent biocompatibility can be readily fabricated. The AIE dots with specific surface functional groups exhibit high emission efficiency, large absorptivity, excellent biocompatibility and strong photo-stability, endowing them ideal for targeting specific cells and/or tissues, and long-term non-invasive *in vitro* and *in vivo* cell tracing. Moreover, some AIE luminogens show aggregation enhanced photodynamic activity and the formulated AIE dots have been used for targeted and imaging-guided photodynamic cancer therapy.

Fabrication of CdTe quantum dots coated SiO_2 and its application in photoluminescence immunosensor

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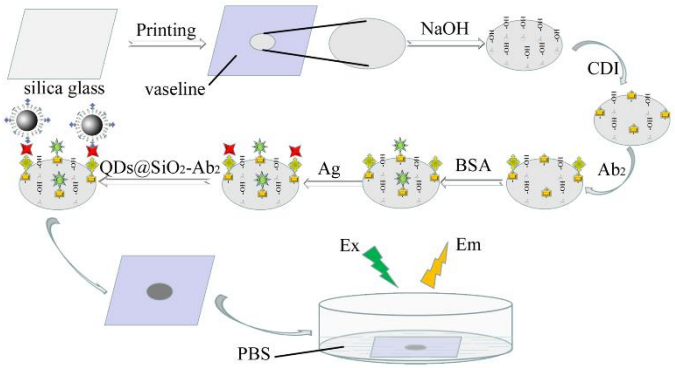
Keywords: CdTe quantum dots; Silica; Photoluminescence; immunosensor; Prostate specific antigen

Recently, kinds of quantum dots (QDs) were synthesized for different purposes. As one species of semiconductor nanomaterial, QDs were famous for its unique photoluminescence properties [1,2]. In this paper, CdTe QDs were synthesized and further assembled on the surface of SiO_2 (QDs@SiO_2). The obtained QDs@SiO_2 was applied in a novel photoluminescence immunosensor for the detection of prostate specific antigen (PSA). The nanoparticals was amino-functionalized using (3-aminopropyl)triethoxysilane and connect with the signal antibody with the addition of glutaraldehyde. Silica glass was selected as the photoluminescence substrate material and was vaseline-printed with pattern. After the silica glass was deal with NaOH and N,N''-carbonyldiimidazole, the capture antibody was fasten on it. Afterwards, immunoreactions were carried through step by step and the labeled Ab_2 can fasten to the silica glass which can be determined by the detection of photoluminescence intensity. The amount of the PSA can be detected in the concentration range of 0.05~50 ng·mL^{-1}, with a limit of detection of 0.01 ng·mL^{-1}. Moreover, the proposed new strategy possesses great potential in other clinical diagnosis.



Scheme 1. Schematic illustration of the fabrication of the photoluminescence immunosensor.

Acknowledgements

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2.5

Catalytic applications of $PtPd@CeO_2$ multicore@shell nanomaterials for the detection of cancer antigen 153

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Keywords: $PtPd@CeO_2$; Electrochemical immunosensor; Cancer antigen 153

Abstract

A facile and feasible strategy was developed to fabricate $PtPd@CeO_2$ multicore@shell nanomaterial [1,2] for the detection of cancer antigen 153 (CA 153). $PtPd@CeO_2$ nanomaterials possessed intrinsic peroxidase-like activity. The as-prepared nanomaterial composed of $PtPd@CeO_2$ nanomaterial showed good adsorption properties for the attachment of secondary anti-CA 153 antibody ($PtPd@CeO_2$-anti-CA 153). With a sandwich-type immunoassay format, the functional $PtPd@CeO_2$-anti-CA153 present good analytical properties to facilitate and modulate the way it was integrated onto the electrochemical immunosensor. The CA 153 immunosensor was fabricated by immobilizing a monoclonal anti-CA 153 antibody (anti-CA 153) on the AuNP attached thiolated graphene on a glass carbon electrode. The sensor interface was characterized using scanning electron microscope, transmission electron microscope, and electrochemical techniques. Under optimized conditions, the linear range of the proposed immunoassay was 0.08-200 U/mL CA 153, the detection limit reached 0.3 ng/mL. Importantly, the as-synthesized $PtPd@CeO_2$ nanomaterial could be further extended for detection of other biomarkers or biocompound.

Acknowledgements

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Therapeutic and Diagnostic Nanoparticles Based on Porous Silicon

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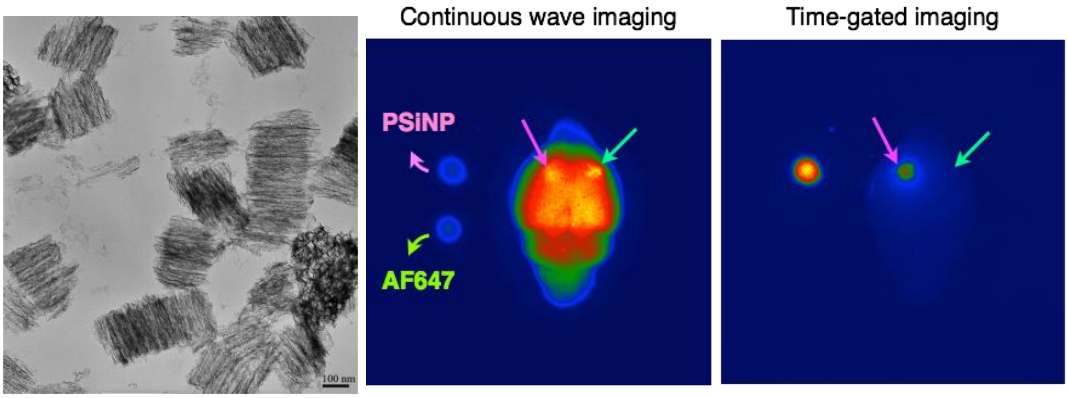
Keywords: drug delivery, photoluminescence, in vivo imaging, cancer**.**

The electronic and optical properties that make the semiconductor silicon so useful for solid-state devices such as solar cells and microelectronics can also be harnessed for biological applications—in particular for *in vivo* imaging and drug delivery. This presentation will present porous silicon-based nanoparticles that enable controlled drug delivery and photoluminescence imaging, using biodegradable drug-loaded porous silicon particles prepared from silicon wafers. The intrinsic photoluminescence that derives from quantum confinement and surface defect states provides a non-toxic and biodegradable luminescent probe for *in vivo* and *in vitro* imaging. The luminescence properties are intimately tied to the surface chemistry of the material, and the relatively long (microseconds) excited state lifetime of this material can be harnessed for time-gated imaging to provide a self-reporting indicator of drug delivery. The Si-H terminated inner surface of the particles is readily modified, enabling the loading of various protein, oligonucleotide, and small molecule therapeutics or combinations.



Porous Si nanoparticles generated by pulsed electrochemical etching of silicon wafers. (left) The particles, on the order of 200 nm, possess intrinsic photoluminescence useful for in vitro or in vivo sensing. (right) Steady-state and time-gated fluorescence microscope images of mouse brain containing porous Si nanoparticles. Intrinsic fluorescence from tissues can be separated from the luminescence of the quantum-confined Si nanostructures by time-gated imaging.[1]

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3.2

Functional Nanoparticles for Tumor Imaging

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Keywords: Tumor imaging, micrometastasis imaging, microenvironment detection

Through either passive or active targeting, functional nanoparticles have shown great potentials in visualizing tumors in vivo. In this presentation, we will present our recent results on tiny tumor imaging, tumor micrometastasis imaging and the visualization of tumor microenvironment as well, apart from the synthesis and surface functionalization of versatile inorganic nanoparticles.

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Lanthanide-Doped Luminescent Nano-Bioprobes for In Vitro Detection of Tumor markers

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Keywords: lanthanide; luminescent nanoprobe; tumor marker; bioassay.

Lanthanide-doped inorganic nanoparticles possess superior physicochemical features such as long-lived luminescence, large antenna-generated Stokes or anti-Stokes shifts, narrow emission bands, high resistance to photobleaching and low toxicity, and thus are regarded as a new generation of luminescent bioprobes as compared to conventional molecular probes like organic dyes and lanthanide chelates. These functional nanoparticles, albeit most of their bulk counterparts were well studied previously, have attracted reviving interest for their biomedical applications in areas as diverse as biodetection, bioimaging, and disease diagnosis and therapeutics. In this talk, we shall focus on the latest advances made in developing lanthanide-doped inorganic nanoparticles as potential luminescent bioprobes, which cover from their chemical and physical fundamentals to bioapplications including the controlled synthesis, surface modification, electronic structure, optical properties, and their promising applications in diverse fields, with an emphasis on heterogeneous and homogeneous in-vitro biodetection of tumor markers [1-7].

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4.1

Bubble-Generating Carrier Systems for Localized Controlled Release

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Keywords: bubble generation, controlled release, drug delivery

In this work, two bubble-generating agents, ammonium bicarbonate (ABC) and sodium bicarbonate (SBC) that can generate CO2 bubbles, are separately encapsulated in carrier systems for actively triggering drug release locally. Widely recognized for their ability to increase intratumoral accumulation, PEGylated liposomes are employed as stable vehicles for carrying doxorubicin (DOX; Doxil®). However, the slow and passive drug release from the Doxil® formulation significantly inhibits its antitumor efficacy. To resolve this problem, our group develops a thermoresponsive liposomal formulation. As the key component of this liposomal formulation, its encapsulated ABC creates the transmembrane gradient needed for a highly efficient DOX encapsulation. Moreover, at a high temperature of roughly 42°C, ABC decomposition generates CO2 bubbles, subsequently creating permeable defects in the lipid bilayer and ultimately inducing a rapid DOX release to instantly increase the drug concentration locally. The feasibility of using this thermoresponsive bubble-generating liposomal system for tumor-specific chemotherapy under mild hyperthermia is investigated. The in vitro drug-release profiles are quantified from test liposomes under mild hyperthermia conditions. Their in vivo biodistribution, pharmacokinetics, drug accumulation, and antitumor activity against locally heated tumors are examined as well. We also develop hollow microspheres (HMs) that can deliver anticancer drug into tumor cells and quickly release the drug in an acidic organelle such as lysosome. The HMs are fabricated from PLGA using a double-emulsion method, with the aqueous core containing DOX and SBC. In acidic environments, SBC reacts with the acid to quickly generate CO2 bubbles, triggering the shell of the HMs to disrupt, thereby quickly releasing DOX locally and causing the cells to die. These highly stimuli-responsive carrier systems contribute to efforts to establish effective tumor-selective chemotherapy.

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Effects of Nano/Micro-Patterned Hydrogels and Nano/Micro Gel Particles on Bone Tissue Engineering

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Keywords: nano/micro-pattern, tissue engineering, hydrogel, particles.

Effects of nano/micro-technology on tissue engineering have been performed by employing micro/nano particles and patterns of hyaluronic acid and chitosan hydrogel. The hydrogel was fabricated by using a Michael type addition reaction mechanism of *in situ* fabrications. Hyaluronic acid and chitosan were in advance derivertized through 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide with acrylic acid and lipoamide as well as tricarboxyethyl phosphines and converted into a hydrogel. By using micr/nano-patterning processing through applications of poly(dimethyl siloxane) substrate, diverse patterns of hyaluronic acid were obtained and were *in vitro* evaluated for its cellular interactions such as adhesion and proliferation by using bone cells. Effects of bioactive molecules and nano/micr-patterns on the bone tissue engineering were evaluated by delivering small molecules such as dimethyloxaloylglycine and sodium butylate. Nano/micro-particles of hyaluronic acid were fabricated in advance by using chemical cross linking agents and bioactive molecules were incorporated into the hydrogel particles. Effects of the bioactive molecules on the cellular behaviors on the patterned gel surface were in vitro evaluated. Effects of bone morphogenic growth factors and mesenchymal stem cells on in vivo bone tissue engineering were also evaluated by using in situ hydrogels in rat calvarial defects model by using diverse analyses such as immunostaining methods.

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4.3

The use of folate-PEG-grafted-hybranched-PEI nonviral vector for the inhibition of glioma growth in the rat

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Glioma is a highly malignant human cancer with very poor survival after treatment. Combined treatment using nonviral agent-mediated enzyme/prodrug therapy and immunotherapy have been suggested an alternative method of cancer therapy. Here we report the cytotoxicity in vitro and the therapeutic efficacy in vivo when the cytosine deaminase/5-fluorocytosine (CD/5-FC) and TNF-related apoptosis-inducing ligand (TRAIL) genes were simultaneously used against rat C6 glioma cells. The potency of the FA-PEG-PEI used as a nonviral vector was tested in the FR-expressed C6 glioma cells and Wistar rats. The C6 glioma cells and animal model were treated by the combined application of FA-PEG-PEI/pCD/5-FC and FA-PEGPEI/ pTRAIL. The antitumor effect was evaluated by survival assays and tumor volume. This study revealed a significant increase of cytotoxicity in vitro following the combined application of FA-PEG-PEI/pCD/5-FC and FA-PEG-PEI/pTRAIL treatments in C6 glioma cells. Animal studies showed a significant growth inhibition of the C6 glioma xenografts using the combined treatment. These results demonstrated that the combined treatment generated additive cytotoxic effect in C6 glioma cells in both in vitro and in vivo conditions, and indicated that such treatment method using both enzyme/prodrug therapy and TRAIL immunotherapy might be a promising therapeutic strategy in treating glioma.

Nano-functionalized Silk for Smart Wearable Devices

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Keywords: Silk, nanomaterials, wearable electronics, biomedical application**.**

With rapid advances of miniaturization and wireless technologies, electronics has been associated with traditional textiles to develop smart wearable devices for daily health monitoring and fitness tracking[1-2]. It is of great demand to fabricate flexible materials that possess both wearability and practical functions for wearable devices.

Silk from Bombyx mori cocoons, a natural protein fiber consisting of 18 amino acids, is considered as an ideal support for wearable electronics because of its softness, high hygroscopicity and superior skin affinity[3], which fulfill the basic requirements of wearable devices on comfort and flexibility. However, practical applications of silk as building components of wearable devices are still rare due to its lack of specific functions such as sensing and conductivity.

In this talk I will first introduce properties and applications of silk, a natural protein fiber with great flexibility, environmental friendliness and excellent mechanical strength. Our research works on surface modification of silk with nanomaterials for antibacterial applications will then be presented. Thirdly, fabrication of a silk fiber sensor for physiological measurements will be discussed. Finally, I will show our recent achievements on the preparation of conductive silk textiles and their application in thermal sensing[4-7].

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4.5

Publishing in Wiley Materials Science Journals

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A highly competitive research environment with increasingly limited research funding has created a “Publish or Perish” attitude among scientists who are judged on the quantity rather than quality of their research articles. This presentation provides a brief overview of current trends and challenges in scientific publishing, some ethical considerations, how publishers and authors interact and influence each other, and how the publishing arena is being transformed. Tips will be presented on how to select an appropriate journal for your paper, what aspects of preparation and presentation to focus on from an editor’s and referee’s perspective, and hints for increasing the discoverability of your paper after publication.

Mesoporous silica nanoparticles: controlled synthesis and biomedical applications

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Keywords: Mesoporous silica nanoparticles, Controlled release, Drug delivery**.**

Drug delivery systems (DDSs) are expected to overcome most of the drawbacks of tranditional cancer thermotherapy by administrating free anticancer drugs. In addition, the multi-drug resistance (MDR) of cancer cells is one of the major causes leading to the failure of cancer chemotherapy, and around two thirds of patients died of the MDR. Mesoporous silica nanoparticles (MSNs) have been found to be capable of efficiently delivering anticancer drugs with sustained and controllable drug release features and possible targeting effects, and now become one of the most attractive research focuses [1-4]. One of the most interesting subjects is the possibility of overcoming MDR by using MSNs-based DDSs.

First, we found that common MSNs-DDS loaded with one kind of anticancer drug is capable of circumventing the drug pump-out mechanism in cytoplasm by MSNs-DDS to a certain extent, and part of the drug released within cytoplasm can diffuse into cell nuclei and thus kill the MDR cancer cells. [5]

By simply pre-loading the hydrophobic or amphiphilic anticancer drugs into the hydrophobic core of the surfactant micelles, a kind of drug@surfactant@MSNs DDS was constructed by the self-assembly between the drug-loaded micelles and silica source. Such a DDS is highly efficient in killing the MDR cancer cells by inhibiting the MDR mechanism[6].

A structure difference-based selective etching strategy was developed to synthesize hollow-structured MSNs (HMSNs) with excellent monodispersity. Different kinds of anticancer drugs, e.g., hydrophobic and hydrophilic drugs, can respectively loaded in the hollow core and the mesopore channels. Such a DDS loaded with more than one kind of drugs was found to be effective in overcoming MDR [7,8] and inhibit the metastasis of cancer cells[9].

Most common DDSs can only deliver drugs into cytoplasm, not directly into the nuclei, while most anti cancer drugs such as DOX act within the nuclei in killing cancer cells. We have found that when the diameter of MSNs is not larger than 50 nm, and MSNs is properly surface-modified with a certain kind of peptide (e.g., TAT), drugs can be directly delivered into the cancer cell nuclei and release therein. Such an intranuclear DDS not only demonstrate enhanced anticancer efficacy for common cancer cells, but can also kill MDR cancer cells with high efficiency [10,11].

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5.2

Microfluidic-based Approaches for Controllable Synthesis of Nanoparticles

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Lipid-covered polymeric nanoparticles (NPs) have been widely used in drug delivery because of their high efficiency and low risk for side effects. Conventional approaches such as emulsion-solvent evaporation, nanoprecipitation and polymerization are either too complex to manipulate or resulting in nanoparticles with a wide size distribution. The rapid mixing and precise control of fluids in the microfluidic chip are helpful to generate nanoparticles of narrow size distribution. We are developing a microfluidic platform that can assemble NPs with a lipid shell and polymeric core in a single-step and applying them to study the mechanisms of the biological effects of nanomaterials. Latest results about the controllable synthesis of lipid-polymeric nanoparticles with microfluidic platform will be presented in this talk.

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Systems Approach to Transform Nanomaterials to Nanomedicines

From Concept to Practice with Nanodrugs for AIDS and Cancer

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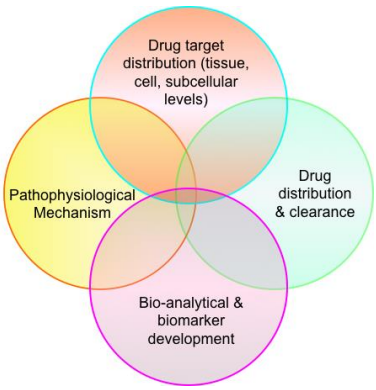
Keywords: HIV, Cancer, anti-retroviral drug combination, cure for AIDS, lymph drug insufficiency

Current drug development paradigm focuses on finding high potency compounds that provide sufficient or sustained therapeutic plasma drug levels to modify disease outcomes. However, a cure for cancer and HIV/AIDS with the traditional approach to maintain therapeutic drug levels achieved limited success. For example, clinical use of highly active oral HIV drug combinations that maintain therapeutic plasma drug levels have been effective in clearing plasma virus to undetectable levels; however, demonstrated insufficient drug levels in lymph nodes, which parallel residual virus persistence (Fletcher et al, 2014, PNAS). The HIV drug-insufficiency finding built on our previous report that HIV patients taking oral indinavir had 3-fold lower mononuclear cell drug concentrations in lymph nodes than in blood (Kinman et al., 2003 JAIDS). Thus, an association of lymph node HIV drug insufficiency and persistence has now been validated. Also $CD4^+$ T cell depletion (HIV pathology) correlates with AIDS disease progression. With established drug targets (lymph nodes) to overcome drug insufficiency in lymphoid cells and tissues, we have developed and employed a "Systems Approach" (see below) to define target profile and engineer multi-drug-incorporated nanoparticles for HIV treatment. The goal is to improve lymphatic HIV drug exposure to eliminate HIV drug-insufficiency and disease progression. We found that nano-particulate drugs that absorb, transit, and retain in the lymphatic system after subcutaneous dosing improve intracellular lymphatic drug exposure, and overcome HIV lymphatic drug-insufficiency. The composition, physical properties, and stability of the drug nanoparticles contribute to the prolonged and enhanced drug exposure in lymphoid cells and tissues. The scale-up friendly lymphatic targeted nanoparticle properties may enable the development of long-acting combination HIV drug therapy to improve patient compliance and outcome. This principle has been extended to design Artemisinin dimer, as well as Gadolinium and Indocyanine green nanoparticles for cancer therapy, high-resolution infrared (IR) and magnetic resonance (MR) diagnostic imaging.



A graphical representation of the **Systems Approach to Nano-Drug Delivery and Targeting.**
The **Systems Approach** to design and develop nanomedicine is based on integration of four areas of biomedical knowledge. (1) Drug target localization information from an intracellular context to cells and tissues as well as organs in the body, (2) knowledge about the biodistribution and clearance of drug candidates in the body over time, (3) the physiological and pathological consequences of the aberration in drug targets that reflects disease progression, and (4) quantitative or bioanalyical markers that could be measured in blood or other samples for predicting drug levels and disease outcomes. These overlapping areas of knowledge and conditions are used to derive a target therapeutic profile for nanomedicine design and evaluation matrices.

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5.4

Targeting gene therapy for tissue fibrosis using an ultrasound-microbubble technique

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Key words: ultrasound-microbubble, gene therapy, Smad7, miR-29, fibrosis.

Tissue fibrosis is a final common pathway leading to the end-stage of organ diseases such as chronic kidney and heart failure, but treatment remains primitive. This is largely due to the lack of strategies to deliver the specific and effective therapeutic drugs/genes locally to the diseased tissues/organs without causing systemic side-effects. To address this fundamental question, we recently developed a safe and effective gene therapy for chronic kidney disease by specifically targeting the TGF-β/Smad signaling (a major pathway leading to tissue fibrosis) locally in the diseased kidney using an ultrasound-microbubble-mediated gene delivery system. For example, in a diabetic kidney disease model, we intravenously inject a mixture of doxycycline-regulated pTRE-Smad7 or pTRE-miR-29b and Tet-ON plasmids with commercially available microbubbles such as Optison or Sonovue in the ratio of 1:1/vol:vol via the tail vein, followed immediately by placing the ultrasound probe on the back skin of the mouse opposite to the bilateral kidneys with a plus-wave output (2 W/cm^2) for a total of 5 min with 30 seconds intervals. After ultrasound treatment, a dose of 200ug/ml of doxycycline is injected intraperitoneally, followed by the addition of doxycycline in the daily drinking water (200ug/ml) for the entire study period. Control ultrasound treatment group has the same protocol but received the $pTRE_2$-Tet-on empty vectors without Smad7 or miR-29b. Smad7 or miR-29b expression within the kidney and therapeutic effects on renal fibrosis were assessed. We found that ultrasound-microbubble treatment largely enhances the gene transfection rate and transgene expression by a 1500-fold increase in Smad7 DNA and a 400-fold increase in Smad7 mRNA expression, which peaks at day 3 and gradually declines to reach insignificant levels by day 28. The higher Smad7 or miR-29b transgene expression was associated with marked inhibition of TGF-β/Smad3 signaling and renal fibrosis, resulting in preservation of renal function. In conclusion, ultrasound-microbubble-mediated local genes therapy appears to be a safe, effective, and specific therapy technique for the organ-specific disease. However, a question whether the modification of the therapeutic drugs with nano-technologies can further enhance the ultrasound-microbubble-mediated therapeutic efficacy locally in the diseased tissues remains to be explored.

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Functionalized boron nitride nanosphere as carrier for enhancing the immunostimulatory effect of CpG oligodeoxynucleotide

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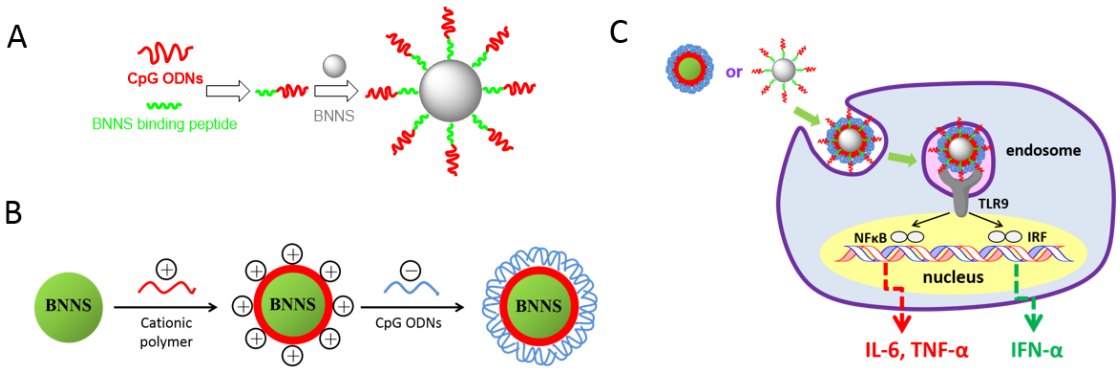
Keywords: CpG oligodeoxynucleotide, boron nitride nanosphere, immunostimulatory effect

Bacterial and viral DNA containing unmethylated cytosine-guanine (CpG) dinucleotides stimulate the mammalian innate immune system. This process is mediated by the activation of Toll-like receptor 9 (TLR9), a member of Toll-like receptor family. Synthetic short, single-stranded oligodeoxynucleotides (ODNs) that contain CpG motifs are similar to those found in bacterial DNA and stimulate a similar immune response. As such, CpG ODNs have potential for clinical applications in the treatment of infectious diseases, allergies, and cancers. However, the immunostimulatory effects are limited by the poor stability and cellular uptake of CpG ODNs. Delivery of unmodified CpG ODNs using carrier nanoparticles is a strategy to improve stability and enhance cellular uptake. With its novel properties and structural similarity to carbon, boron nitride (BN) has received considerable scientific interest. BN has the advantage of high biocompatibility, with easier cellular uptake and lower toxicity than carbon. Previous results showed that BN nanosphere (BNNS) had little cytotoxicity, and protected unmodified CpG ODNs from degradation by serum nucleases. In addition, BNNS taken up by cells localized to endolysosomes, and this localization was maintained even after cell division. This was particularity advantageous, since TLR9 also localizes to endolysosomes. However, the loading capacity of CpG ODNs on the surface of BNNS was not sufficient to induce a robust cytokine response. Therefore, their immunostimulatory effect was also limited. In the present work, we developed novel delivery systems for CpG ODNs through functionalization of BNNS. We first identified a peptide with high affinity for BNNS, then we used this peptide as linker molecule to enhance the loading of CpG ODNs on BNNS. Next, we used the cationic polymer, such as chitosan and polyethylenimine to functionalize BNNS and obtain the postitive surface charge which make it easier to bind the nagetive-charged CpG ODNs. These delivery systems greatly improved the loading capacity and cellular uptake of CpG ODNs and increased the interaction between CpG ODNs and TLR9. They are proved to be effective in enhancing the immunostimulatory effect of CpG ODNs.



Schematic illustration of construction of BNNS-based CpG ODNs delivery systems (A,B) and their enhanced immunostimulatory effect (C).

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6.1

Stimuli-regulated Cancer Theranostics Based on Magnetic Nanoparticles

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Keywords: Magnetic Nanoparticles, Diagnosis, Phototherapy, MRI, Stimuli**.**

Magnetic nanoparticles (NPs), which possess controlled size, shape and magnetic moments, have been applied as multifunctional probes in biomedical field, including MRI, drug delivery and magnetic hyperthermia, by enhancement of contrast in magnetic resonance imaging (MRI) and emote manipulation.[1]

In this talk, we will first present general protol of monodisperse magnetic NPs, and then give an example of hollow manganese phosphate (HMP) NPs with particle size of 18 nm and a 10 nm hollow structure, for pH-modulated cancer cell targeted MRI and drug delivery. [2] Folic acid (FA) was selected as a target molecular for specific binding with cancer cells, and doxorubicin was loaded into the hollow structure for cancer therapy. This multifucntional probe can specifically target cancer cells overexpressing FA receptors, and be engulfed by lysosomes. The HMP NPs were dissolved at low pH environment in lysosomes, which can release Mn^{2+} for sensitive MRI, and DOX loaded for effective killing of cancer cells. [3]

We then talk about Hagg iron carbide (Fe_5C_2) magnetic NPs for bimodal tumor imaging and therapy (Scheme). [4-6] Interestingly, due to the presence of carbon layers of NPs, with high absorption in near-infrared (NIR) optical region, Fe_5C_2 NPs can be used for photoacoustic tomography (PAT) and photothermal therapy (PTT). The probe exhibits high saturation magnetization, r_2 relaxivity and temperature increasing after exposure to NIR. The conjugation of Herceptin enabled the targeting to Her2-overexpressed cells (SK-OV-3 cells). After incubation with NPs in vitro, SK-OV-3 cells showed much lower MRI T_2 signal, and no noticeable in vitro toxicity has been observed. Determined by using a fluorescent viability stain, cells incubated with NPs and exposed to NIR light were found to have undergone photothermally induced morbidity. The in vivo experiments were carried out on nude mice with ovarian cancer modal. After injection of NPs through the tail vein, it showed long-lasting negative-contrast enhancement MRI as well as high PAT signal at the tumor site. High tumore ablation was achieved after NIR irritation. From the loss of body weight, morphological and pathological examinations, almost no systematic toxicity has been observed. Our results highlight the great potential of Fe_5C_2 NPs as a multifunctional probe for cancer theranostic applications.

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Subcellular Behaviors Evaluation of Nanopharmaceuticals with Aggregation-Induced Emission Molecules

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Keywords: nanopharmaceuticals, aggregation-induced emission, aggregation-caused quenching, intracellular behaviors

Nanopharmaceuticals own myriad advantages for diseases treatment, not only in delivering the therapeutic agents, but also in deciphering their innate intracellular or subcellular behaviors, and providing detailed diagnostic and prognostic information, quantifying treatment efficacy and designing better therapeutics. To evaluate subcellular behaviors of nanopharmaceuticals, the colorful fluorescence is the best candidate, which is capable of painting the subcellular details in three dimensions with high resolution. Otherwise, the fluorescence is switchable, so that the subcellular details can be lightened specifically without undesirable background. However, most nanopharmaceuticals themselves lack of fluorescent report group, which needs extra steps to be introduced. Not only that, the introduced fluorescent groups also suffer concentration quenching or aggregation-caused quenching (ACQ) when they are embedded in nanopharmaceuticals with high concentration. The unique aggregation-induced emission (AIE) effect provides a straightforward solution. Opposite to ACQ molecules, AIE molecules are always hydrophobic, and do not undergo the ACQ effect even in high concentration. Hence, the AIE molecules can be directly introduced as building blocks to provide the driven force for self-assembly of nanopharmaceuticals, and allowing us to develop label-free, ACQ-free and luminescent nanopharmaceuticals that can implement the drug delivery and subcellular behaviors evaluation simultaneously. It can inspire the scientists to develop next generation nanopharmaceuticals that can be guided by fluorescence imaging and thus realizing the concisely controllable drug delivery.

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6.3

Novel nano-theranostics based on human serum albumin

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Keywords: Nano-theranostics, Human serum albumin , Photothermal therapy, Cancer metastasis treatment

Nanomaterials especially functional inorganic nanomaterials exhibit a range of unique inherent physical and chemical properties useful in biomedicine. Starting from 2009, our research group has been working on the development of functional nanomaterials including sp2 carbon nanomaterials (carbon nanotubes and graphene), rare earth up-conversion nanoparticles (UCNPs), organic nanoparticles, and multifunctional composite nanostructures for applications in multimodal biomedical imaging, drug and gene delivery, as well as novel photo-therapies of cancer. In the meantime, we have also devoted considerable efforts to investigate the biological effects and toxicology of various nanomaterials at both cellular and animal levels. Aiming at future clinical translation of our technology, in the recent two years we have started to look into the use of natural biomaterials as building blocks to construct novel types of nano-theranostic agents. Human serum albumin (HSA), the most abundant protein in human blood, has been extensively used as a biocompatible drug carrier. In this talk, I would like to introduce our latest efforts to develop multifunctional tumor-targeted nanomedicine for imaging-guided combination therapy of cancer based on HSA, which is a rather old drug delivery system but shows new promises in our recent research.

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Self-assembled Porphyrins for Applications in Imaging and Drug Delivery

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Keywords: Porphyrins, nanoparticles, imaging, therapy, theranostics

Porphyrins have played important roles in development of approaches to the diagnosis and treatment of diseases, in particular based on how these molecules interact with light. This lecture will cover some of our recent efforts to develop new self-assembled materials from porphyrins and related molecules and how these nanomaterials have potentially advantageous properties for disease diagnosis and therapy.

In particular, several recently reported nanoscale systems will be discussed that are being investigated preclincally.

First, porphyrin nanovesicles have been developed that can release drugs in response to red laser irradiation, leading to enhanced drug deposition in irradiated tumors. Inclusion of 2 molar % porphyrin-phospholipid (PoP) imparts optimal near infrared (NIR) light-triggered release of doxorubicin (Dox) from conventional sterically stabilized stealth liposomes. Dox in stealth PoP liposomes has a circulation half-life in mice of 21.9 hours and is stable in storage for months. Following intravenous injection and NIR irradiation, Dox deposition increases ~7 fold in treated subcutaneous xenografts. A low dose 3 mg/kg Dox phototreatment with stealth PoP liposomes was more effective than a maximum tolerated dose of free (7 mg/kg) or conventional long-circulating liposomal Dox (21 mg/kg). To our knowledge, Dox-loaded stealth PoP liposomes represent the first reported long-circulating nanoparticle capable of light-triggered drug release.

Second, these porphyrin nanovesicles can be chelated with cobalt for simple functionalization using polyhistidine ligands. Methods to attach polypeptides to lipid bilayers are often indirect, ineffective and can represent a substantial bottleneck in the formation of functionalized lipid-based materials. Although the polyhistidine tag (his-tag) has been transformative in its simplicity and efficacy in binding to immobilized metals, the successful application of this approach has been challenging in physiological settings. Here we show that lipid bilayers containing porphyin-phospholipid that is chelated with cobalt, but not other metals, can effectively capture his-tagged proteins and peptides. The binding follows a Co(II) to Co(III) transition and occurs within the sheltered hydrophobic bilayer, resulting in essentially irreversible attachment in serum or in million-fold excess of competing imidazole. Using this approach we anchored homing peptides into the bilayer of preformed and cargo-loaded liposomes to enable tumour-targeting without disrupting the bilayer integrity. As a further demonstration, a synthetic HIV-derived protein fragment was bound to immunogenic liposomes for potent antibody generation for an otherwise non-antigenic peptide.

Finally, we will discuss other emerging approaches to developing high-density porphyrin-related polymers for theranostic indications. For example, a family of highly light-absorbing naphthalocyanine nanoparticles have been developed for safe and real-time gastrointestinal imaging following oral administration.

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7.2

Carbon Dots for Photodynamic and Photothermal Therapy

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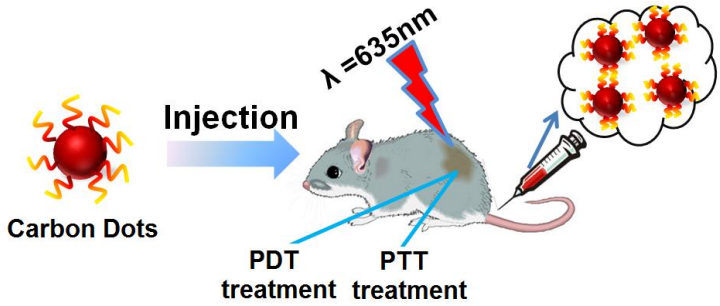
Keywords: Carbon Dots; Photodynamic Therapy; Photothermal Therapy

Phototherapy, which is often used to treat cancers, includes photodynamic therapy (PDT) and photothermal therapy (PTT). Considerable efforts have been exerted to develop light-triggered nanomaterials with PDT or/and PTT effects.[1,2] Very recently, we have prepared graphene quantum dots (GQDs) by using polythiophene derivatives as the carbon source. The as-prepared GQDs exhibited high $^1O_2$ generation capability (about 130%), which could be applied as a photodynamic therapy (PDT) agent for efficient cancer therapy.[3] In the present work, we prepared a brand-new C-dots using another conjugated polymer, polythiophene benzoic acid (PBA), as the precursor. The prepared C-dots exhibited dual simultaneous photodynamic and photothermal effects under 635 nm laser irradiation with a $^1O_2$ generating efficiency of 27% and high photothermal conversion efficiency of up to 36.2%. To the best of our knowledge, this study is the first to demonstrate the use of C-dots for combined PDT and PTT therapies *in vivo* by using a single red laser (Scheme 1).



Scheme 1. C-dots for combined PDT and PTT therapies *in vivo*.

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AIE Probes for Biomedical Applications

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Keywords: AIE, ROS, photodynamic therapy, biosensing, bioimaging

Fluorogens with aggregation-induced emission (AIE) characteristics have recently aroused significant research interest. The unique AIE process offers a straightforward solution to the aggregation-caused quenching problem faced by traditional fluorophores and photosensitizers. Our recent work has discovered that certain AIE fluorogens have enhanced reactive oxygen species generation in solid state.[1] In this talk, we summarize our recent AIE work to highlight the utility of AIE effect in the development of new fluorescent bioprobes for image-guided photodynamic therapy (PDT), which allows the use of highly concentrated fluorogens for biosensing, imaging and therapeutic applications. Molecular probes based on AIE fluorogens (AIEgens) with photodynamic activity offer direct visualization of specific analytes and biological processes in aqueous media while the AIE dot-based bioprobes with surface functionalized targeting elements show advanced features over quantum dots and small molecule dyes.[2] In addition, the AIE probes can effectively generate ROS to kill targeted cells upon appropriate light irradiation, which find applications in cancer therapy. In this talk, I'll bring you to the wonderful world of AIEgens, with special focus on their biomedical applications.

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7.4

Molecular Engineering of Photofunctional Materials for Biological Applications

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Keywords: photoinduced electron transfer, nanocarbon materials, gold nanorod, light

The integration of chemistry and biology has paved the way for new interdisciplinary science and technology that enable the control and manipulation of functions of biological systems. This methodology has been extended to explore the fusion between tailored materials and biological systems as well as protein machines and artificial systems. The representative examples involve the control of ion channels by photochemical switching and the use of biomolecular motors and pumps interfaced with synthetic systems.

Controlling cell functions using external photoresponsive nanomaterials has enormous potential for the development of cell-engineering technologies and intractable disease therapies, but the former currently requires genetic modification of the target cells. The biomedical applications of carbon nanomaterials, such as carbon nanotubes, single-walled carbon nanohorns, and fullerenes, have enormous potential in current biomedical research, disease diagnosis and therapy. Among these carbon nanomaterials, single-walled carbon nanotubes (SWNTs) have remarkable optical properties of effectively absorbing near-infrared light (NIR, λ = 650–900 nm) at their M_{11} band of the metallic SWNTs (m-SWNTs) and the S_{22} band of the semiconducting SWNTs (s-SWNTs). Nevertheless, to our knowledge, the biological activities depending on m- and s-SWNTs have never been examined. Here we report on the first comparison of the photothermal effect (PTE) and photodynamical effect (PDE) of chirality-enriched m-SWNTs and s-SWNTs. Under NIR laser irradiation, s-SWNTs generated reactive oxygen species (ROS) more than m-SWNTs, whereas m-SWNTs produced heat more efficiently than s-SWNTs. More importantly, cancer cell killing by PDE of s-SWNTs has been disclosed.

The photocontrol of neuronal cells could provide an appealing optogenetic method; for instance, such localized stimulation by NIR illumination might potentially be utilized as a non-invasive therapeutic modality. However, current optogenetic approaches generally require prior genetic modification of the target cells, which limits their broad application. The transient receptor potential vanilloid type 1 (TRPV1) is a Ca^{2+} permeable polymodal channel gated by noxious physical and chemical stimuli, including heat (>43˚C), low pH values (<5.2), capsaicin, and the Euphorbia toxin resiniferatoxin. We present a method using plasma-membrane-targeted gold nanorods (pm-AuNRs) prepared with a cationic protein/lipid complex to activate a thermosensitive cation channel, TRPV1, in intact neuronal cells. Highly localized photothermal heat generation mediated by the pm-AuNRs induced Ca^{2+} influx solely by TRPV1 activation. In contrast, the use of previously reported cationic AuNRs that are coated with a conventional synthetic polymer also led to photoinduced Ca^{2+} influx, but this influx resulted from membrane damage. Our method provides an optogenetic platform without the need for prior genetic engineering of the target cells and might be useful for novel TRPV1-targeted phototherapeutic approaches.

Finally, we focus on nanoscale electric field of a photogenerated charge-separated (CS) state of a donor-acceptor linked molecule. If this CS molecule can be incorporated unidirectionally into the intact biological membrane and then the CS state is generated by photoinduced electron transfer (ET), the extremely large electric field (~10^6 V cm^{-1}) of the photogenerated CS state will affect voltage-gated ion channel, resulting in the switching of ion transport across the membrane. We chose ferrocene (Fc)-porphyrin (H_2P)-C_{60} linked triads as the CS molecule, because the ability of generating a long-lived CS state efficiently. Delivery of the CS molecules to the plasma membrane of PC12 cells by a membranous nanocarrier and subsequent light irradiation led to the depolarization in the membrane potential as well as the inhibition of potassium ion flow across the membrane.

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Effects of gold nanorods on eliminating the amyloid-β aggregates with laser irradiation

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Keywords: Amyloid fibrils, gold nanorods, femto-second laser

The pathogenesis of Alzheimer's disease (AD) is associated with the aggregation of the amyloid-beta (Aβ) peptides into toxic aggregates. How to inhibit the aggregation of Aβ peptides or eliminate the aggregates that are already present has been an urgent problem, and intensive efforts have been made in past decades. Here, gold nanorods (Au NRods) which exhibit high cross section of light absorption in the near infrared region are attempted for providing local high temperature fields when exposed on femto-second laser. Their effects on the amyloid aggregates with laser irradiation are investigated by atomic force microscopy (AFM) and transmission electron microscopy (TEM). The results reveal that almost all of Aβ fibrils are broken into small filaments with the irradiation of 818 nm femto-second laser pulse for 60 s. On the contrary, with the irradiation of continuous-wave laser for same time at same power density, most Aβ fibrils keep well after the treatment. From the investigation of TEM, it is found that the femto-second laser irradiation for 60 s can generate the explosion of Au NRods and melt to amorphous components, resulting in the disaggregation of amyloid aggregates. Furthermore, the irradiation of Aβ fibrils can reduce their toxicity on SH-SY5Y cells compared with non-irradiation sample. So our results demonstrate that the ultrafast laser treatment can efficiently destroy the amyloid aggregates in the presence of Au NRods, providing an efficient and rapid-treat method on eliminating Aβ fibrils.

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8.1

Targeted Destruction of Cancer Stem Cells by Nanomedicine

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Keywords: cancer stem cells; nanomedicine; microfluidics.

Our research interests focus on the study of cancer cell communications and the development of nanotechnology to detect and destruct cancer cells. Recently, we have investigated the interaction and inter-conversion between cancer cells and the so-called cancer stem cells (CSCs), which consist of a small subset of cells responsible for sustaining tumorigenesis and drug resistance. We have developed a microfluidic system for co-culturing cancer cells and studying the effects of microenvironments on cell growth, migration and interactions. We have also developed multifunctional nanoparticles by integrating specific antibodies for targeting CSC surface markers, magnetic cores for externally activated heat generation, and chemotherapeutic agents for interrupting specific pathways in the CSCs. Our results showed that *in vitro* cancer cell growth and *in vivo* tumor growth were effectively inhibited by the nanomedicine through the combined effects of thermotherapy and chemotherapy.

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A simple and sensitive fluorescence method for activity analysis and effects screen in vitro and vivo of Mung Bean Nuclease based on graphene oxide

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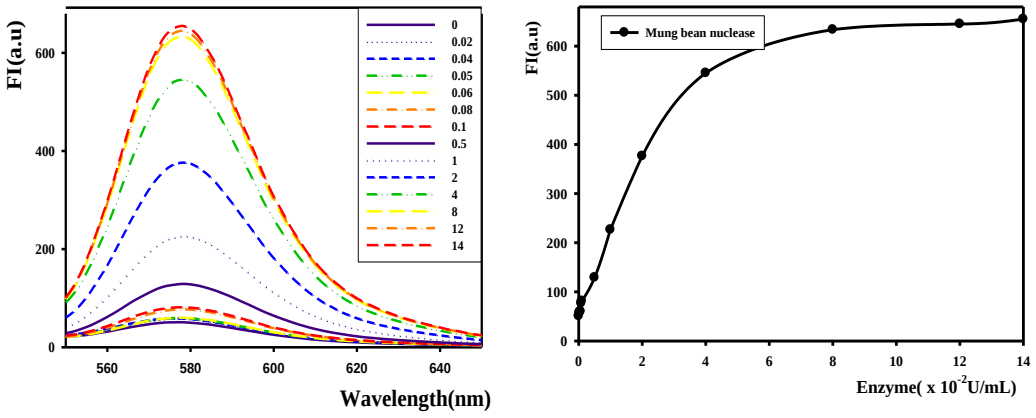
Keywords: Mung bean nuclease, graphene oxide, fluorescence probe, antibiotics

The activity level of Mung bean nuclease can be used as an important marker for monitoring the plant's growth and development. Herein, an ultra-high sensitive fluorescent sensing platform for this nuclease is developed based on the different affinity of graphene oxide (GO) with single-stranded DNA containing different numbers of bases in length. In the absence of Mung bean nuclease, the adsorption of the fluorophore-labeled ssDNA on GO results in high efficiency quenching of fluorescence due to the close proximity of the fluorophore to GO surface. Conversely and very importantly, Mung bean nuclease can cleave the dye-labeled ssDNA into small fragments and the introduction of GO into the sensing solution results in weak quenching of the fluorescence due to the weak affinity of the short fluorophore-labeled oligonuleotide fragment to GO, and the change of fluorescence intensity is tightly related with increasing concentration of Mung bean nuclease. Mung bean nuclease can be detected in a range of 2×10^{-4} to 4×10^{-2} unit/mL with a detection limit of 0.5×10^{-4} unit/mL under the optimal conditions. In addition, we used this sensor to investigate the effects of metal ions and antibiotics on this enzyme in vitro and found that some of them influence the enzyme's activity in a type and concentration-dependent manners. Moreover, the effect of inhibitors on Mung bean nuclease was further confirmed by in vivo experiment and anticipated fluorescence signals are obtained. Interestingly, we found that the inhibiting of this enzyme can significantly reduce the growth speed of Mung bean seedling. Overall, the reported data not only widen our knowledge of the enzymatic properties and biofunction of Mung bean nuclease, but also indicate that the simple, rapid and sensitive method can be hopefully accelerate high-throughput detection of samples and drug screening of this enzyme *in vitro* and *in vivo.*



A B

Fig.1 Activity assay of Mung bean nuclease. Panel A shows representative wavelength scan curves obtained from $2x10^{-4}\sim4\times10^{-2}$ U/mL Mung bean nuclease respectively. Panel B shows the final fluorescence intensity of enzymatic products as a function of the concentration ofenzyme. [GO-P]=100 nM.

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8.3

Rapid, Multiplexed, Mobile Phone-Enabled Point of Care Diagnostic Device to Detect Infectious Diseases

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Keywords: nanomaterial, diagnostic, lab-on-chip**.**

Medical countermeasures surveillance and reporting during and after a public health emergency event require sensitive and specific detection/diagnostic methods and devices. We are designing, building, and testing a rapid, multiplexed, mobile phone-enabled diagnostic device to detect dengue virus, Ebola virus, and yellow fever virus. The goal is to deliver a device that will permit screening for multiple pathogen markers without the need for refrigeration, specialized training, specialized equipment or chemicals. Mobile phone technology is used to analyze the lateral flow data, quantify the results, and upload the results for real time epidemiology.

The device is based on lateral flow chromatography, an established technology. The platform for multiplexed pathogen detection is using multi-colored silver nanoplates. This design requires no external excitation source and permits multiplexed analysis in a single channel, facilitating integration and manufacturing. Nanoparticle surface chemistry is being evaluated to identify low cost approaches to prepare conjugated nanoparticles. A mobile phone app has been coded to record the image of the multiplexed diagnostic, correct the image for user photography errors, quantify the signal intensities, and upload data to a server, with GIS. A prototype device that detects and distinguishes the four serotypes of dengue virus, dengue IgG/IgM, Ebola glycoprotein, and yellow fever NS1 protein has been built and tested. Initial specificity and sensitivity tests using laboratory proteins and human patient serum samples are favorable. A multiplexed rapid lateral flow diagnostic for field use detects pathogens and uploads data for real time epidemiology.

Fig*: A new paper diagnostic device can detect Ebola and other viral hemorrhagic fevers in about 10 minutes. The device has silver nanoparticles of different colors that indicate different diseases. On the left is the unused device, opened to reveal the contents inside. On the right, the device has been used for diagnosis; the colored bands show positive tests*

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2D and 3D Surface Enhanced Raman Scattering (SERS) Substrate for Real Application

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Keywords: 2D structure, 3D structure, Surface Enhanced Raman Scattering.

Abstract: Due to the large enhancement of weak Raman signals, Surface-Enhanced Raman Scattering have shown great application in diverse field, such materials sciences, biology, nanotechnology, chemical and biological sensing detection etc.

To achieve low cost, large-scale fabrication and high reproducibility of SERS substrate, different technology such as electron beam lithography, focused ion beam pattering, plasma etching and others, had been explored. The main structure for SERS substrate could be 2D and 3D structure, such as ZnO nanopillar, polymer Nanofingers and others. The polymer-based 2D and 3D structure for fabrication and application of SERS substrate become more attractive due to the easy fabrication processes and low cost. In this talk, the polymer-based 2D (Figure 1) and 3D (Figure 2) SERS substrate were presented and shown in below SEM images.

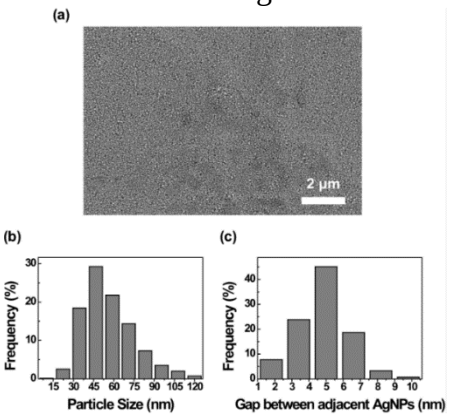

Figure 1. 2D SERS substrate: a) high cover density AgNPs monolayer; B) and C) particle size distribution and gap between adjacent AgNPs, respectively.

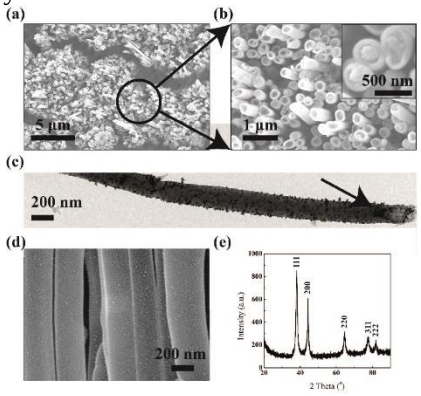

Figure 2. 3D SERS substrate: a) Top-view SEM image of PE nanotubes showing a large scale fabrication; b) HRSEM image of PE nanotubes decorated with AgNPs on the top; c) TEM image of PE nanotube; d) Cross-section SEM image of PE nanotube e) XRD pattern of PE nanotubes with AgNPs monolayer.

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9.1

Engineering biointerface with controlled cell adhesion towards cancer diagnostics

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Keywords: Circulating tumor cells, biomolecular recognitions, bio-inspired interfaces, cell capture/release.

Circulating tumor cells (CTCs) have become an emerging "biomarker" for monitoring cancer metastasis and prognosis. Although there are existing technologies available for isolating/counting CTCs, the most common of which using immunomagnetic beads, they are limited by their low capture efficiencies and low specificities. By introducing a three-dimensional (3D) nanostructured substrate – specifically, a silicon-nanowire (SiNW) array coated with anti-EpCAM – we can capture CTCs with much higher efficiency and specificity. The conventional methods of isolating CTCs depend on biomolecular recognitions, such as antigen-antibody interaction. Unlikely, we here proposed that nanoscaled local topographic interactions besides biomolecular recognitions inspired by natural immuno-recognizing system. This cooperative effect of physical and chemical issues between CTCs and substrate leads to increased binding of CTCs, which significantly enhance capture efficiency. Recently, we have also developed a 3D cell capture/release system triggered by aptamer enzyme, electrical potential and Temperature, which is effective and of "free damage" to capture and release cancer cells. The bio-inspired interfaces of cell capture and release open up a light to rare-cell based diagnostics, such as CTCs, fetal cells, stem cell and so on (**Fig. 1**).

Fig. 1 Design and application of multiscale biointerface with controllable cell adhesion

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High Luminescent Organic Dye Nanoparticles for Bioimaging

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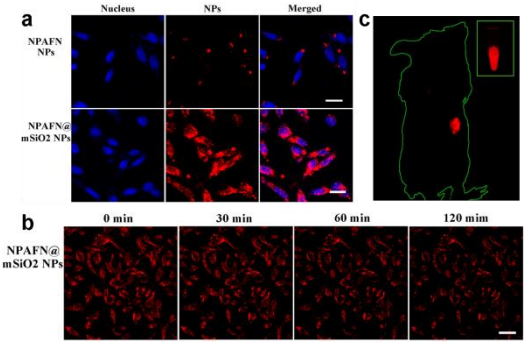
Keywords: Fluorescent dye nanoparticles, bioimaging, in vitro, in vivo



We report a new strategy of using carrier-free pure dye nanoparticles (NPs) to achieve highly luminescent fluorescent probes for in vitro and in vivo imaging. For traditional aggregation-induced quenching (AIQ) dyes, the dye NPs can be used not only as carriers to encapsulate different doped dyes, but also as fluorescence resonance energy transfer donors to couple with the doped dyes (as acceptors), to achieve multicolor luminescence with amplified emissions (AE). The resulting optimum green emitting NPs show high brightness with quantum yield (QY) of up to 45% and AE of 12 times; and the red emitting NPs show QY of 14% and AE of 10 times. These highly-luminescent doped NPs can be further surface modified with poly(maleic anhydride-alt-1-octadecene)-polyethylene glycol (C18PMH-PEG), endowing them with excellent water dispersibility and robust stability in various bio-environments covering wide pH values from 2 to 10. Applications of the NP probes in in vivo and ex vivo imaging are also investigated. Intense fluorescent signals of the doped NPs are distinctly, selectively and spatially resolved in tumor sites with high sensitivity.

For dyes with the characteristics of aggregation-induced emission enhancement (AIEE), near-infrared (NIR) dye NPs (NPAPF) show more than ten-times enhanced fluorescent emission with QY up to 14.9%, large stokes shift as well as much more superior photostability than conventional dyes (FITC). We also further introduce surface roughness onto the NPs by developing core/shell silica-coated structures. Systematic studies indicate surface roughness can dramatically induce over ten-fold enhancement in fluorescence signals when compared with those having a smooth surface. Cellular internalization mechanism studies show that these NPs with rough surfaces enter cells through the specific non-clathrin- and non-caveolae-mediated pathways. Such pathways enable the NPs to enter cells very quickly. Moreover, their unique cellular entry pathways also make them possess high lysosomal escape capability, which results in significantly reduced cellular excretion rate. These combined merits of enhanced cellular uptake efficacy and decreased cellular excretion endow the fluorescent dye NPs as a potential probe for highly sensitive bioimaging, particularly for real-time and long-term tracking of cells.

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9.3

Conjugation of Ultrasmall Iron Oxide Nanoparticles onto Multifunctional Dendrimers for SPECT/MR Dual-Mode Imaging of Gliomas

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Keywords: dendrimer,ultrasmall iron oxide, radionuclide ^{99m}Tc, Gdchelates, SPECT/MR dual-modeimaging

Development of multifunctional nanoplatforms for dual-mode or multimode imaging of cancer, especially the combination of radionuclide- and non-radionuclide-based imaging modes still remains a great challenge. Here, we report the preparation, characterization, and utilization of multifunctional dendrimer-based nanoplatform for dual-mode single-photon emission computed tomography (SPECT)/magnetic resonance (MR) imaging of gliomas (Figure 1). In our study, amine-terminated generation five poly(amidoamine) dendrimers (G5.NH_2) were used as a platform to sequentially modify with Gd chelator (DOTA), polyethylene glycol (PEG)-linked RGD peptide, and fluorescein isothiocyanate (FI), acetic anhydride to partially acetylate the remaining dendrimer terminal amines, followed by conjugation with citric acid-stabilized ultrasmall iron oxide (Fe_3O_4) NPs, chelation with Gd(III), and final radiolabeling with ^{99m}Tc. The formed multifunctional nanoprobe of G5.$NHAc_{25}$-FI-*m*PEG-(PEG-cRGD)-DOTA-Gd-Fe_3O_4-^{99m}Tc was characterized *via* different techniques. We show that the nanoprobe before ^{99m}Tc labeling is cytocompatible and hemocompatible in the given concentration range, and able to target a model glioma cell line overexpressing $\alpha_v\beta_3$ integrin *in vitro*. Significantly, the RGD-targeted multifunctional nanoprobe enables efficient targeted SPECT/MR dual mode imaging of cancer cells *in vitro* and a xenografted tumor model *in vivo via* an active RGD-mediated targeting pathway. With the facile dendrimer nanotechnology that enables dendrimers to be functionalized with different biological ligands, the developed dendrimeric nanoprobe may hold great promise to be used as a dual mode SPECT/MR probe for imaging different biological systems.

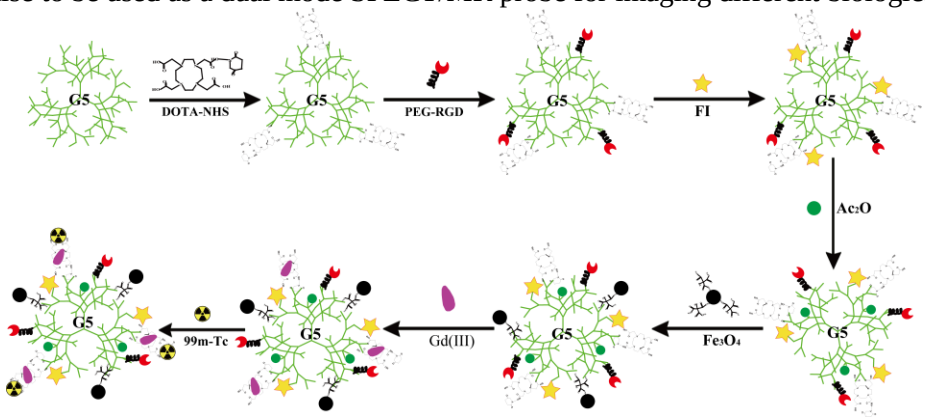

Figure 1. Schematic illustration of the preparation of the G5.$NHAc_{25}$-FI-*m*PEG-(PEG-cRGD)-DOTA-Gd-Fe_3O_4-^{99m}Tc nanoprobe.

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Virus-Mimetic Nanovesicles as a Versatile Antigen Delivery System

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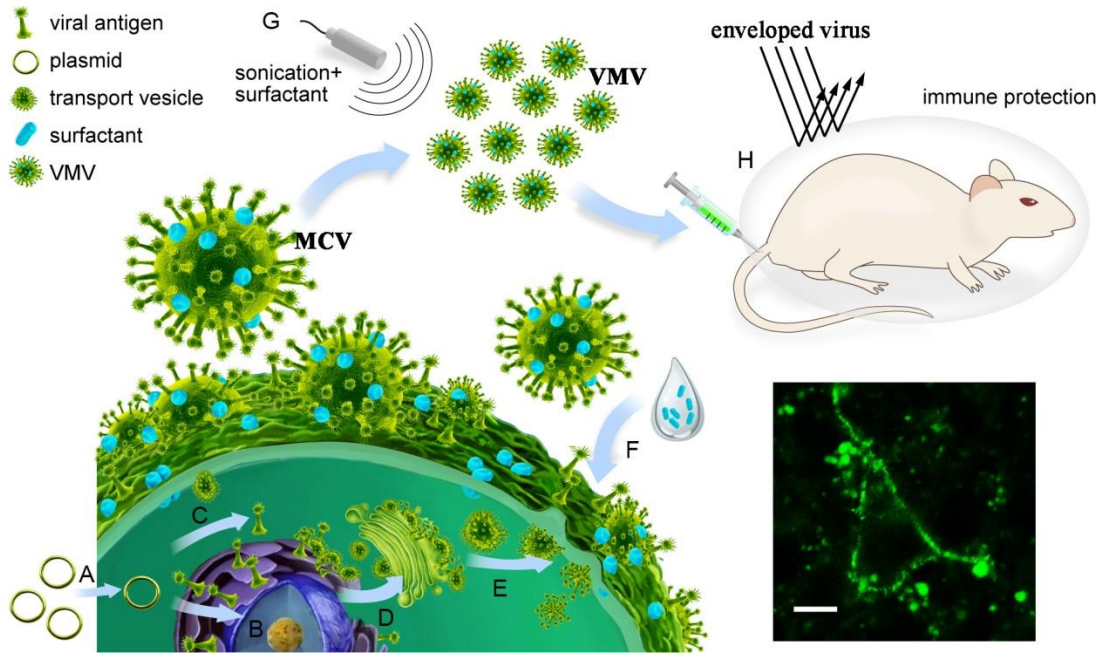
Keywords: Virus-mimetic nanovesicle; nanobiotechnology; nanovaccine; antigen delivery system; cell membrane

It is a critically important challenge to rapidly design effective vaccines to reduce the morbidity and mortality of unexpected pandemics. Inspired from the way that most enveloped viruses hijack a host cell membrane and subsequently release by a budding process that requires cell membrane scission, we genetically engineered viral antigen to harbor into cell membrane, then form uniform spherical virus-mimetic nanovesicles (VMVs) that resemble natural virus in size, shape, and specific immunogenicity with the help of surfactants. Incubation of major cell membrane vesicles with surfactants facilitated to generate a large amount of nano-sized uniform VMVs displaying the conformational epitopes. The protein integrated into VMV by its hydrophobic transmembrane peptide has more modifications such as glycosylation than ones in conventional subunit vaccines. Moreover, many viral envelope glycoproteins can be genetically engineered onto VMV liposomal surface so as to mimic the properties and conformational epitopes of natural virus. With the diverse display of epitopes and envelope glycoproteins that can be functionally anchored onto VMVs, we demonstrate VMVs to be straightforward, robust and tunable nanobiotechnology platforms for fabricating antigen delivery systems against a wide range of enveloped viruses.



Schematic showing the preparation process of virus-mimetic nanovesicles (VMV) for anchoring epitopes or enveloped-virus glycoprotein to VMV surface.

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10.2

Anti-cancer Nanotherapeutics: smart delivery, efficacy and toxicity

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Abstract

Nanotherapeutics are promising vectors for smart drug because multiple moieties can be conjugated to achieve targeted delivery. Cancers are notoriously difficult to control because of their abilities to grow and metastasize by forming new blood vessels and to become drug resistance by the efflux of chemotherapeutics. To combat cancer, there are two important targets, namely to block the angiogenesis process and to overcome the efflux-mediated multidrug resistance. In addition, the biocompatibility of these nanotherapeutics have to be investigated with *in vitro* and *in vivo* toxicological investigations. We summarise our series of experiments on using nanotherapeutics as anti-cancer agents here. Functionalized carbon nanotubes (f-CNTs) entered the nucleus of mammalian cell lines in a dynamic and bidirectional manner, and did not cause discernible changes. In the model organism zebrafish, f-CNTs circulated in the blood vessels and were cleared out of the body after 24 hours. To achieve smart delivery of these multimodal drugs, f-CNTs were conjugated to the antiangiogenesis drug thalidomide, a peptide cyclic RGD for angiogenesis-specific targeting, and a fluorescent marker. This antiangiogenic nanomedicine inhibited ectopic angiogenesis in zebrafish xenografted with human tumors which were proangiogenic. Multidrug resistance (MDR) is a major clinical obstacle to the success of cancer chemotherapy. We explored the applicability of f-CNTs as carriers for drug resistant cells. The f-CNTs penetrated into mammalian cells without damage to the plasma membranes and its accumulation did not affect cell proliferation nor cell cycle progress. More importantly, these f-CNTs accumulated in the multi-drug resistance cancer cells as efficient as in the sensitive cancer cells, showing that multi-drug resistant cells failed to remove the intracellular f-CNTs. We also explored the applicability of gold nanoparticles (AuNPs) as carriers for efficient drug delivery in cancer cells which are resistant to cancer drugs. We first developed a gold-doxorubicin (AuNPs-DOX) nanoconjugates system to overcome MDR. Intracellular uptake and accumulation of AuNPs-DOX was greater than that of free DOX in the MDR cell, resulting in enhanced cytotoxicity against MDR cancer cells. These studies highlight the potential of using AuNPs and f-CNTs as smart drug delivery systems for anti-angiogenic therapy and for overcoming of MDR in cancer.

Surface Ligand in Modification and Assembly of Multifunctional Nanoparticles for Biomedical Applications

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Keywords: Surface ligand, Nanoparticles, Self-assembly, Bioimaging, Drug delivery

Nanotechnology has received extraordinary attention recently due to its burgeoning role in pharmaceutical research. The materials composing the nanoparticles produce fascinating and diverse functionalities as a result of their exceptionally small size. Size control, both during synthesis and in particle suspensions, is a sine qua non for functionality. This can be accomplished by masking the particle surface with a multitude of different ligands [1, 2]. Ligands are essentially fungible and can be exchanged at various times to confer the desired properties to the particle. This can include protecting the particle from harsh aqueous conditions [3, 4], such as pH extremes, maximizing optical properties for diagnostics or shielding the particle from potentially hostile conditions found in the body. The design of the ligand can have crucial effects on biodistribution as well as evasion of biological defenses. Ligands can even be designed to provide new functionality in response to various environmental stimuli to improve their therapeutic or diagnostic capabilities [5, 6]. Clever combination of different nanoscale materials via ligand directed self-assembly will lead to the development of multifunctional nano-biomedical platforms for advanced drug delivery system such as simultaneous targeted delivery, fast diagnosis, and efficient therapy [7-9].

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10.4

Interfacial assembly and theranostic applications of organic-inorganic hybrid nanomaterials

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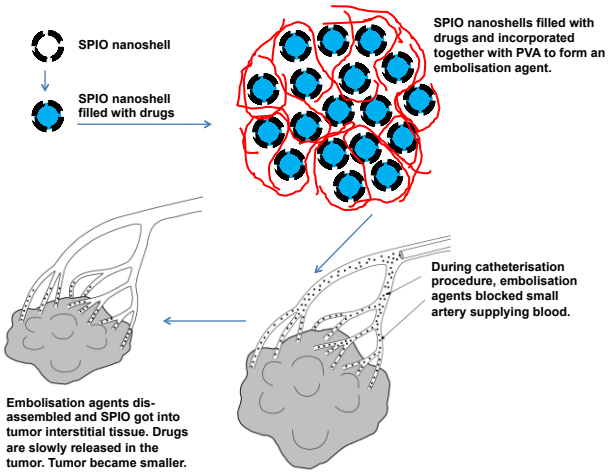
Keywords: cancer, hollow structure, iron oxide, polymer, porous

Nanotheranostic materials have been recently involved the use of nanoparticles for simultaneous diagnostic and therapeutic purposes. New materials have been extensively developed towards drug delivery and tumor imaging. In the first part of the presentation, the synthesis, characterization, and properties of theranostic nanoparticles based on organic-inorganic hybrid nano-particles will be described.[1-4] The hybrid nanoparticle consists of a superparamagnetic iron oxide core and a series of coatings which are stimuli-responsive supramolecules or polymers. By the concept of nanovalve based on supra-molecular gate-keepers, stimuli-responsive drug delivery nanosystem was synthesized by (i) modified solvothermal reaction; (ii) sol-gel reaction; and (iii) coupling reaction of supramolecules. In these systems, the "ON/OFF" switching of the gatekeeper supramolecules can be controlled by pH-sensitive intramolecular hydrogen bonding or electrostatic interaction (such as metal chelating). Biological evaluation of the nanoparticles renders them non-cytotoxic and can be uptaken by several cell types. The anti-tumor drug (doxorubicin) loading and release profiles which were studied by the UV/visible absorption spectroscopy, were demonstrated by using ultrasonic wave. Magnetic resonance imaging analysis of the particles reveals a high relaxivity, rendering them useful nanotheranostic agents. Another part of the presentation will focus on design, synthesis, purification, and property-exploration of mono-functionalized gold nanoparticles.[5]



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Design of 3S Transition-Nanocarriers for Cancer Drug Delivery Cascade

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Keywords: nanomedicine, cancer drug delivery, function integration**.**

The cancer drug delivery process is a cascade of five steps consisting of circulation in blood, accumulation and penetration into the tumor, cellular internalization and intracellular drug release, or the CAPIR cascade. Thus, the most challenging aspect of cancer nanomedicine design is the integration and synchronization of all functions required to accomplish the CAPIR cascade into one system, particularly, many of which are in opposite in different CAPIR steps. Here, we present the design of nanocarriers capable of size, surface and stability property (3S) transitions essential for accomplishing the CAPIR cascade, enabling the carried drug to reach cells deep in the tumor and circumvent the drug resistance, significantly enhancing its in vivo antitumor efficacy.

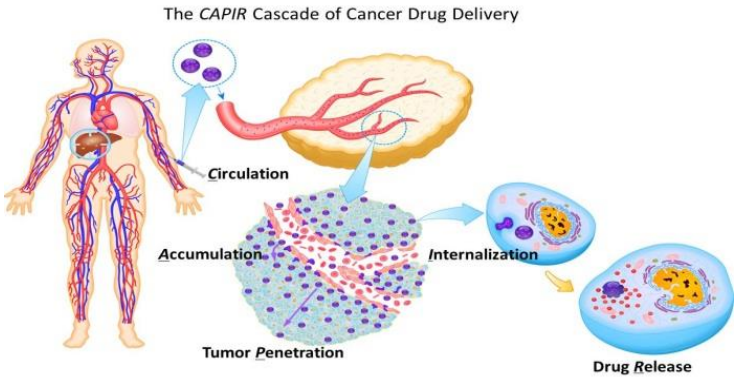

Fig. 1 The CAPIR cascade of cancer drug delivery—A cascade of five steps: circulation in the blood compartments, accumulation in the tumor from the hyperpermeable tumor vessels, penetration into the deep tumor tissue to reach all tumor cells and subsequent internalization by them, and finally intracellular drug release.

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11.2

Tracking single viruses infecting their host cells using quantum dots

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Keywords: Track, virus, infection, live cell, quantum dot**.**

Single-virus tracking (SVT) technique, which uses the microscopy to monitor the behaviors of viruses, is a vital tool to study the real-time and in-situ infection dynamics and virus-related interactions in live cells. To make SVT a more versatile tool, we have developed quantum dot (QD)-based SVT technique, which can be utilized for long-term and high-sensitivity tracking of viruses to invade their host cells. In this presentation, we will describe the QD-based SVT technique developed in our group, including the QD labeling strategy, instrumentation, and image analysis, and its application in elucidating the mechanism of the invasion of viruses into their host cells. We will mainly emphasize how to use this technique to acquire more key real-time information about virus infection by making full use of the advantages of QDs as a tag in the SVT.

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Diamond Nanointerface for Signal Dissection in Live Neuronal Cells

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Understanding such signaling cascades and network within cells has been the core topic in modern biology. Great efforts have been made to develop novel tools for probing and analyzing intracellular signaling in living cells with sufficient sensitivity, specificity and spatial/temporal resolution. A major barrier for these tools to access intracellular regions is the cell plasma membrane. Many existing methods are limited in different regards, including safety concerns, varied efficiencies and cytotoxicity in different types of cells, laborious experimental protocols or low throughput. Here, we demonstrate a novel platform for interfacing with live neuronal cells by utilizing arrays of diamond nanoneedles. Using this technique, cellular membrane is disrupted by arrays of nanoneedles with a force on the order of a few nano-newtons, which is controlled by centrifugation-induced supergravity, to achieve reliable intracellular access without damaging cells. We have shown that this technique is applicable to deliver a broad range of molecules and materials into neurons, including small chemicals, antibodies, quantum dots, nanoparticles, and DNAs, in a high throughput manner. In addition, this nanointerface has also been adopted as a minimally invasive method for in situ probing specific signaling components of cellular innate immunity in living neurons. Upon functionalization with aptamer-based molecular sensors, the nanoneedles were inserted into cytoplasmic domain to capture molecular targets of transcriptional factor, NF-κB. Notably, the delivery and probing based on our diamond nanointerface can be repeatedly performed with a reversible protocol to enable dynamic studies that were not possible with traditional methods involving the use of cell homogenates.

11.4

Interaction of Nanodiamond with Cells: characteristics, implication, and applications

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Keywords: Nanodiamond, shape effect, endosome escape, drug delivery, bio-sensing

The cellular evolution of Nanoparticles (NPs) refers to NP's uptake, intercellular translocation and excretion. It is vital to application of nanoparticles in cell imaging, bio-sensing, drug delivery, suppression of drug resistance, gene delivery, and cytotoxicity analysis. In the present work, we take nanodiamond (ND) as an example, and disclose specific features in its interactions with cells. We demonstrate that the morphology of ND independently determined their cellular fate. A more general conclusion is that NPs with sharp shapes, regardless of their surface chemistry, size, or composition, could pierce the membranes of endosomes that carried them into the cells and escape to the cytoplasm, which in turn significantly reduced the cellular excretion rate of the nanoparticles. We will also discuss the implication and application of such features for gene delivery, subcellular targeting, and biosensing. This work is supported by CRF of RGC (Project No. CUHK4/CRF/12G), and the National Basic Research Program of China (973 Program) under Grant No. 2014CB921402.

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The effect of carbon nanotubes on the aggregation of amyloid-β peptides

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Keywords: amyloid peptides, protein aggregation, carbon nanotubes

The aggregation of β-amyloid peptides (Aβ) is taken as the main possible cause of the Alzheimer's diseases (AD). How to inhibit the aggregation of Aβ peptides has been intensively concerned in the last decades. Here the effects of single wall carbon nanotubes (SWCNTs) on the aggregations of $A\beta_{1-40}$ are investigated. The results demonstrate that the presence of SWCNTs would result in the quick adsorption of $A\beta_{1-40}$ monomers and oligomers on their surfaces and stacking into multilayer continually, which plays an important role in inhibiting the formation of mature fibrils. In addition, the effect of SWCNTs on the fibrotic $A\beta_{1-40}$ aggregates is also investigated. It is found that the injection of SWCNTs to the solution which contain long fibrils can significantly disintegrate the long fibrils to short filaments or oligomers by atomic force microscopy (AFM) and ThT fluorescence, indicating SWCNTs can efficiently damage the formed aggregates of $A\beta_{1-40}$. As a results, our results suggest that SWCNTs can act as a promising candidate for inhibiting the aggregation of $A\beta_{1-40}$ peptides, as well as for breaking aggregated β-sheet fibrils.

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12.1

Core-Shell Upconversion Nanoparticle@Metal-Organic Framework Nanoprobes for Luminescent/Magnetic Dual-mode Targeted Imaging

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Keywords: core-shell UCNP@Fe-MIL-101_NH_2 nanostructures, surface modification, UCL/MRI dual-mode targeted imaging, biocompatibility, in vivo and in vitro

Abstract

Multifunctional core-shell nanostructures made of inorganic nanoparticles (NPs) integrated with metal-organic frameworks (MOFs) have attracted much attention in recent years.[1] Nanoscale metal–organic frameworks (NMOFs), a class of hybrid materials composed of metal ions and organic bridging ligands, have emerged as a promising platform for designing multifunctional materials for biomedical applications, owing to their tunable composition, rich pore size and volume, easy functionalization, flexible network or accessible metal sites, good biocompatibility and biodegradability.[2] In this work, we present a novel strategy for preparation of core-shell upconversion nanoparticle@MOF nanostructures in which a $NaYF_4$:Yb,Er upconversion nanoparticle (UCNP) core is coated with amino-functionalized octahedral iron carboxylate NMOF shell (Figure 1 a-e). The X-ray diffraction (XRD) pattern reveals two sets of characteristic peaks and further confirms that the products are composed of crystalline Fe-MIL-101_NH_2 proved by excellent agreement with the theoretical powder pattern of Cr-MIL-101 at low angles of 1.5°-15° and the hexagonal phase UCNPs at high angles of 15°-70°. Impressively, the well-defined core-shell UCNP@Fe-MIL-101_NH_2 nanostructures combine the near-IR optical properties of the UCNP cores and the T_2-MRI property of the NMOF shells (Figure 1 f-i). Both the UCL emission spectrum and the relaxation response of suggest that they are a good candidate for UCL/MR imaging. Moreover, after conjugated with PEG and folic acid, the core-shell nanostructures are demonstrated as high-resolution nanoprobes for the tumor-targeted dual-modal luminescence/MR imaging both in vitro and in vivo (Figure 2). Considering the wide variety, unique properties, and broad applications of both UCNPs and MOFs, we believe the construction strategy of core-shell nanostructures will open up new avenues to integrate advantages of both UCNPs and MOFs for many biological applications, including multimodality imaging, photoregulated drug release, and image-guided targeted cancer therapies.

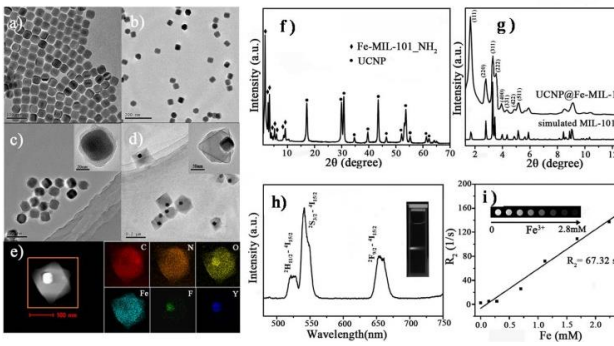

Figure 1. The TEM, XRD of UCNP@Fe-MIL-101_NH_2 and the near-IR optical and magnetic properties

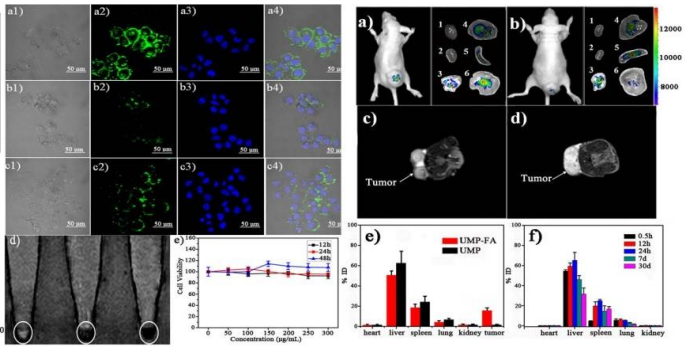

Figure 2. Dual-modal UCL/MR of UCNP@Fe-MIL-101_NH_2 in vitro and vivo imaging

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Nanomaterials for Two-photon Imaging and Phototherapy

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Keywords: two-photon excitation, bio-imaging, photodynamic therapy, energy transfer, Plasmon resonance

Photodynamic therapy is a promising noninvasive treatment of cancers and other diseases. Two-photon excitation PDT (TP-PDT) is advantageous over the traditional one-photon counterpart by offering deeper penetration into body tissues, more confined treatment area and 3-dimensional spatial selectivity to reduce adverse effects to nearby normal tissue. However, the clinical applications of TP-PDT are limited by the small two-photon absorption cross sections of current photosensitizers. A lot of research efforts have been devoted to the development of novel two-photon photosensitizers with large two-photon absorption cross sections.

Here I will present our recent research work on development of various nano-photosensitizers that allow simultaneous two-photon imaging and photodynamic therapy with enhanced efficiency. We used two strategies to develop composite nanomaterials with enhanced two-photon properties. One is based on energy transfer from conjugated polymers with two-photon absorption cross sections, which acted as two-photon light harvesting materials to transfer the absorbed energy to photosensitizers. We have developed photosensitizers doped conjugated polymer nanoparticles that display large two-photon absorption cross section, high emission yield and singlet oxygen generation capability, selectively cancer cell targeting and killing capability at the same time [1]. The second approach is based on plasmon resonance enhancement. We have developed various plasmon engineered nanocomposites with enhanced two-photon properties for simultaneous two-photon imaging and photodynamic therapy [2]. The exceptional properties of these nano-photosensitizers render them great potentials for high spatial resolution imaging-guided TP-PDT.

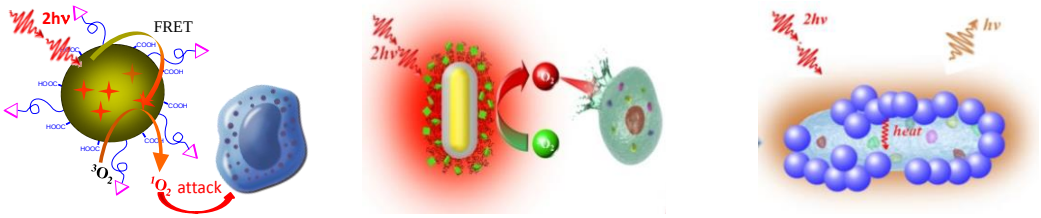

Figure 1. Various schemes for simultaneous two-photon imaging and two-photon photodynamic therapy.

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12.3

Highly sensitive colorimetric detection of protein O-GlcNAcylation based on gold nanopartilce-catalyzed signal amplification

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Keywords: Gold nanoparticles; O-GlcNAc detection; Colorimetric assay; Cancer cell

O-GlcNAcylation, a new type of post-translational modification of proteins, plays an essential role in various cellular processes and is closely related to some fatal diseases such as cancers. An advanced method is greatly desired to efficiently analyse O-GlcNAc and further elucidate its key biological roles. In this project, a highly sensitive colorimetric assay method was described for O-GlcNAc detection based on use of spherical gold nanaoparticles as a label, in which colloidal gold catalyzed the copper deposition on its surface in the presence of Cu^{2+} and ascorbic acid, resulting in gold@copper core-shell nanoparticles. After addition of $FeCl_3$ solution, the deposited copper reduces Fe^{3+} to Fe^{2+}, which then reacts with bathophenanthroline disulfonic acid disodium salt to form red coordination complexes. The intensity of the produced red color is directly related to the level of O-GlcNAc. As expected, the O-GlcNAc was successfully detected by naked eyes or by mesurement of UV-vis absorbance. To validate these results, O-GlcNAc levels in normal and cancer cell lines were successfully analysed by the developed colorimetric sensor. In addition, effect of OGA inhibitor on protein O-GlcNAcylation was also evaluated with same sensing systems. The developed sensor is applicable for rapid, colorimetric and sensitive O-GlcNAc detection, providing a promising analytical approach for glycomics research and cancer diagnostics.

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Circularly polarized photocatalytic activity in gold-nanogap-silver chiroplasmonic nanoparticles

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Keywords: chiroplasmonic; circularly polarized photocatalytic activity; gold-nanogap-silver; nanoparticles

The strong plasmonic chiroptical activities of gold core-DNA-silver shell nanoparticles (NPs) are reported for the first time, using cytosine-rich single-stranded DNA as the template for the guidance of silver shell growth. The anisotropy factor of the optically active NPs at 420 nm reaches 1.93×10^{-2}. Their chiroptical properties are likely induced by the DNA-plasmon interaction and markedly amplified by the strong electromagnetic coupling between the gold core and silver shell.

Gold-gap-silver nanostructures (GGS NSs) with interior nanobridged-gaps were enantioselectively fabricated. Guided by L/D-cysteine, the GGS-L/D (L/D represents L/D-cysteine) NSs showed reversed plasmon-induced circular dichroism (CD) signals in the visible region. It was found that the nanogap played a key role in the plasmonic CD of GGS NSs. And the chiroptical response could be tailored by adjusting the amount of cysteine. The anisotropy factor of GGS-L/D NSs with a 0.5 nm interior gap at 430 nm was as high as ~0.01. The circularly polarized photocatalytic activity of GGS NSs was discovered that under the irradiation of left-circularly polarized (LCP) light, the catalytic efficiency of GGS-L NSs was 73-fold and 17-fold more active than that of Au nanoparticles (NPs) and Au@Ag core-shell NPs, respectively. While under the right-circularly polarized (RCP) light, the catalytic activity of GGS-D NSs was about 71 times and 17 times higher than that of the NPs as noted above, respectively. This unique chiral nanostructures with high plasmonic response could be applied to enantioselective catalysis.

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Abstract of Posters

A carrier-free strategy to fabricate nanoparticles for chemo-photodynamic synergistic therapy

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Keywords: carrier-free, nanoparticles, synergistic therapy

Drug delivery system boomed quickly, which pushed great development of controlled release. Carrier-free drug delivery systems had tremendous advantages.[1] We developed a new carrier-free nanoparticles self-assembled from mPEG-Porphyrin conjugates for synergistic therapy. [2] mPEG-Porphyrin was not only a photosensitizer drug but also a drug carrier for doxorubicin loading. This facile nanoparticles combined chemo and photodynamic therapy for cancers. The conjugates were characterized by NMR, MS and GPC. The morphology of nanoparticles was observed via AFM and TEM. DOX was efficiently encapsulated in the nanoparticles, π-π stacking interaction between drugs and carriers played an important role for the contribution of high drug loading content. In vitro and in vivo results revealed the drug-loaded nanoparticles exhibited excellent anti-tumor effect and achieved dual chemo-photodynamic therapy.

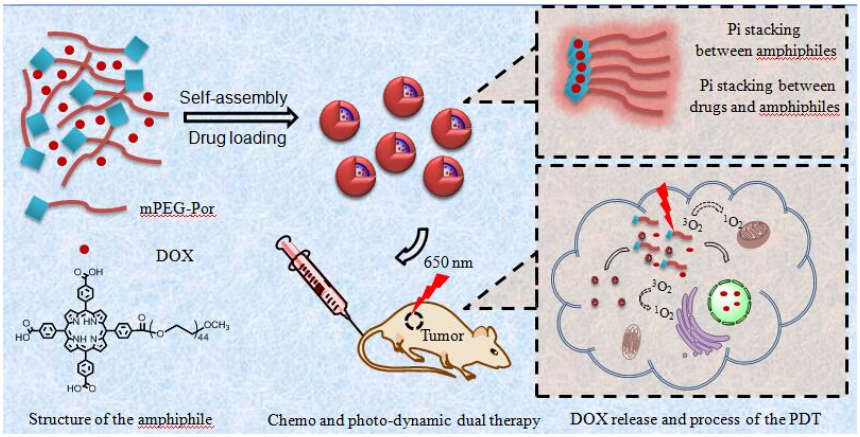

Figure 1. Schematic illustration to show the structure of the amphiphile, and the combination of chemo-photodynamic therapy.

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P-02

Ag/Si nanowire array embedded microfluidic chips: an in-situ surface enhanced Raman spectroscopy monitoring platform

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Keywords: Keywords: Microfluidic, Reproducibility, Biomolecule detections, Nanowires array**.**

The incorporation of surface enhanced Raman spectroscopy (SERS) detection into microfluidic channels enables fast, damage-free and information-rich sensing and analysis, and it thereby triggers considerable research interests. However, conventional SERS systems are depend on narrow spacing with intense electromagnetic fields and usually surfer from low reproducibility, especially in the presence of dynamic liquids. In this paper, we report the fabrication of Ag/Si nanowire (NW) array embedded microfluidic chips as an in-situ SERS monitoring platform. This on-chip SERS system not only provides highly reproducible SERS signals in liquid based detection, but also is capable of large bio molecule detection, demonstrated by the detection of R6G and natural source double strand DNA, respectively. Such excellent SERS performances are attributed to the wide range and uniform enhancement field yielded by the propagating surface plasmon on ordered Ag/SiNW structure upon laser illustration. Using a combined photolithography and nanosphere-lithography (NSL) technique, we incorporated this newly developed Ag/SiNW SERS substrate with microfluidic channels, forming a highly-efficient SERS-active mirofludic chip. The increased surface area in the nanowire array facilitates uniform adsorption of analytes. Moreover, the wide-range electric field of Ag/SiNWs reduces the influence of molecule movements in fluctuating liquid. Benefited from this, even coated with an interfere layer of molecules before application, reliable signals of analytes can still be obtained. In addition, it also makes the detection of large molecules conveniently achievable. Furthermore, to demonstrate the advantage of incorporating multi-functions on a chip, we investigated the application of using such a system for real time monitoring of a model reaction, nitrite detection on this SERS-active microfluidic chip.

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P-03

Protective Autophagy in AgNPs Associated Radiotherapy for Glioma

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Keywords: Silver nanoparticles; Autophagy; Glioma; Radiation sensitization; Cell signaling pathways

Treatment for malignant glioma, which is the most aggressive intracranial tumor (approximately accounts for 50%) and the most lethal of all cancers, is still facing rigorous challenge. Ionizing radiation is the gold-standard adjuvant treatment for malignant glioma. But in the clinical course, high grade gliomas, particularly glioblastoma multiformes, show high resistance to radiotherapy and chemotherapy, which lead to the poor prognosis that patients with glioblastoma with a median survival of only 14.6 months.

Autophagy is a highly conserved catabolic process which regulates the degradation of intracellular components and long-lived proteins in lysosomes. It could be induced by many kinds of exogenous stimulation such as nano materials. There are three possible effects of elevated autophagy: pro-survival, pro-death, or neutral. However, the function of autophagy in the tumor therapy, especially in radiotherapy, is still unclarified.

Nano materials has been more and more widely used in tumor treatment due to its unique physicochemical properties, specifically in radiosensitization, chemosensitization and integrated cancer diagnosis and treatment. AgNPs, owing to their excellent surface enhanced Raman scattering and broad-spectrum antimicrobial activities, are now attracting great interests for a wide range of biomedical applications. Recent studies have also shown that AgNPs have excellent anti-tumor effect through the mechanisms involving oxidative stress, DNA damage, cell cycle arrest, apoptosis or necrosis. What's more, AgNPs could also be used as a sensitizer for radiotherapy, the radiosensitivity enhancing effect of AgNPs on glioma both in vitro and in vivo had been demonstrated in the previous studies of our group, but the underlying mechanism by which AgNPs could enhance the radiation sensitivity remains to be elucidated.

In the present study, the relationship between autophagy induced by AgNPs and their radiation sensitivity enhancing effect for clinically relevant MV X-rays was studied. First of all, AgNPs at the size of 15.47 ± 3.98 nm was synthesized, a size and dose dependent antitumor effect and significant radiosensitivity enhancing effect of the particles were observed, which was consistent with previous studies. We also found that cell protective autophagy could be induced by AgNPs and/or radiation, which was verified by the use of 3-MA. Furthermore, inhibitors of ERK and JNK pathways was employed to assess some possible pathways through which AgNPs induced autophagy and improved the outcomes of radiotherapy. By inhibiting ERK and JNK with U0126 and SP600125 respectively, we found that the autophagy level of the glioma cells treated with AgNPs and radiation were attenuated. Moreover, SP600125 down-regulated the apoptosis rate of the co-treated cells significantly, but U0126 had not showed this effect.

Taken together, the data provided strong support for the conclusion that autophagy played a protective role in the cells treated by AgNPs with/without radiation, and JNK signaling pathway was also involved in the experiment system. Furthermore, understanding the autophagy should be essential to the clinical applications of AgNPs and could potentially be exploited for new therapeutic strategies in glioma radiotherapy.

These findings have been published on Biomaterials 62(0): 47-57.

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P-04

Layered Double Hydroxide Nanoparticles for Drug Delivery and Bioimaging

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Keywords: Layered double hydroxide nanoparticles, drug delivery, bioimaging, cancer therapy

Nanomaterials and nanotechnology have received tremendous attentions in applications of electronics, photonics, energy, biology and medicine. In this poster, we mainly focus on layered double hydroxide (LDH) nanomaterials for drug delivery and bioimaging applications.

In this poster, we describe layered double hydroxide (LDH) nanoparticles for bioimaging and drug delivery applications. Firstly, we demonstrate pristine LDH nanoparticles can be used as filler to enhance the mechanical strength of dissolving polymer microneedles for better skin penetration. Also, we fabricate a novel highly luminescent covalently bonded LDH–sodium fluorescein dye nanohybrid. This nanocomposite shows a significantly higher quantum yield (QY) of 55.1% in comparison with the nanohybrids prepared using previously reported anion exchange (3.0%) and coprecipitation (12.4%) methods. Folic acid conjugated self-assembled LDH nanoparticles can enhance selectivity and efficacy for drug delivery: folic acid conjugated self-assembled LDH nanoparticles have a drug loading capacity of 27 wt% and are able to enter cell nuclei and dramatically improve the efficacy of MTX.

In summary, we describe LDH nanoparticles for biomedical application. The results will be beneficial for developing next generation of advanced drug delivery systems for future clinical applications.

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P-05

Terminal moieties effects on the drug delivery properties of PEG-PCL polymeric micelles

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Keywords: Polymeric micelle, Conjugated moieties, Drug delivery, Chrysin, π-π stacking interaction

Polymeric micelles, which were self-assembled from amphiphilic copolymers, are the representative vehicles for drug delivery [1]. We know that π-π stacking interaction is one of the main driving forces for the supramolecular self-assembly due to strong interaction within π-π conjugated segments [2]. Anticancer drug doxorubicin contains aromatic moieties as anticancer drugs [3], it is understandable that the increase of interactions between anticancer drugs and the core of polymeric micelles will equip a greater thermodynamic driving force for drug loading [4]. In this study, doxorubicin was loaded in PEG-PCL micelles with the terminal modification of cinnamic acid, coumarin, and chrysin, which had π-π conjugated structures. The terminal moieties effect on the drug delivery properties was investigated. Both in vitro and in vivo results showed that the bigger end group on micelles exhibited better anti-tumor efficacy.

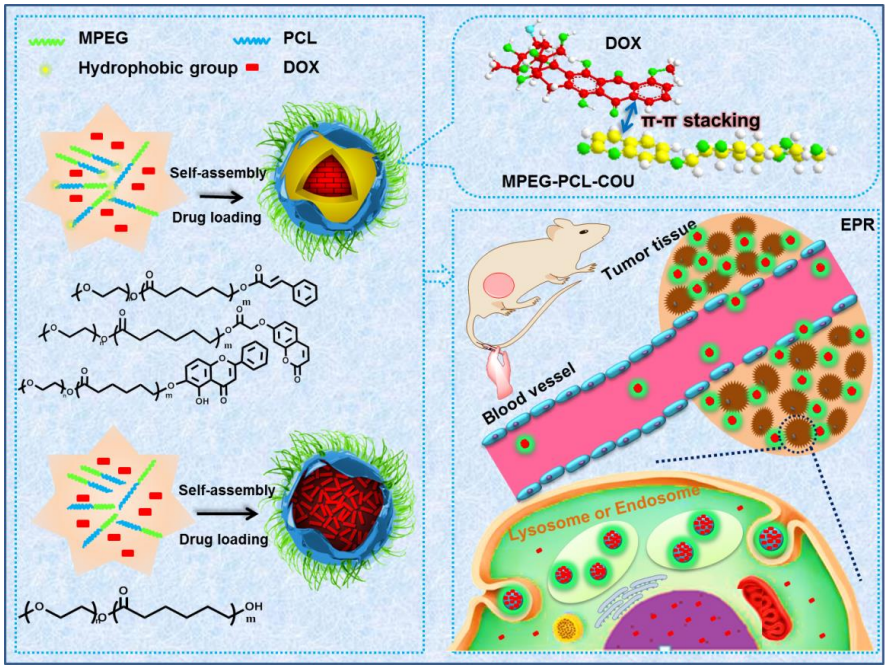

Figure 1. Schematic illustration of polymeric micelles with different end group as a lipophilic moiety for anticancer drug doxorubicin delivery.

Acknowledgement
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P-06

Self-Monitoring and Self-Delivery of Photosensitizer-Doped Nanoparticles for Highly Effective Combination Cancer Therapy *in Vitro* and *in Vivo*

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Keywords: self-monitoring, self-delivery, FRET, combination therapy, *in vitro* and *in vivo*

Theranostic nanomedicine is capable of diagnosis, therapy and monitoring the delivery and distribution of drug molecules and has received growing interest. Herein, a self-monitored and self-delivered photosensitizer-doped FRET nanoparticle (NP) drug delivery system (DDS) is designed for this purpose. During preparation, a donor/acceptor pair of perylene and 5,10,15,20-tetro (4-pyridyl) porphyrin (H_2TPyP) is co-doped into a chemotherapeutic anticancer drug curcumin (Cur) matrix. In the system, Cur works as a chemotherapeutic agent. In the meantime, the green fluorescence of Cur molecules is quenched (OFF) in the form of NPs and can be subsequently recovered (ON) upon release in tumor cells, which enables additional imaging and real-time self-monitoring capabilities. H_2TPyP is employed as a photodynamic therapeutic drug, but it also emits efficient NIR fluorescence for diagnosis via FRET from perylene. By exploiting the emission characteristics of these two emitters, the combinatorial drugs provide a real-time dual-fluorescent imaging/tracking system in vitro and in vivo, and this has not been reported before in self-delivered DDS which simultaneously show a high drug loading capacity (77.6%Cur). Overall, our carrier-free DDS is able to achieve chemotherapy (Cur), photodynamic therapy (H_2TPyP), real-time self-monitoring of the release and distribution of the nanomedicine (Cur and H_2TPyP). More importantly, the as-prepared NPs show high cancer therapeutic efficiency both *in vitro* and *in vivo*. We expect that the present real-time self-monitored and self-delivered DDS with multiple-therapeutic and multiple-fluorescent ability will have board applications in future cancer therapy.

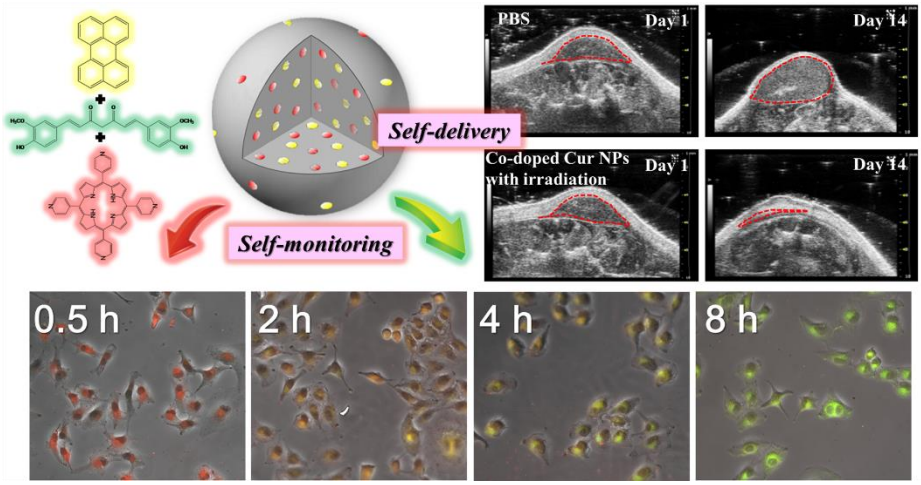

Fig. 1 Schematic illustration on the preparation of the H_2TPyP (photosensitizer, acceptor) and perylene (donor) co-doped Cur NP and its application for self-delivered and self-monitored chemo-photodynamic theranostics.

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Preparation and Preliminary Application of Magnetic Nanocrystal/Polymer Composite Beads

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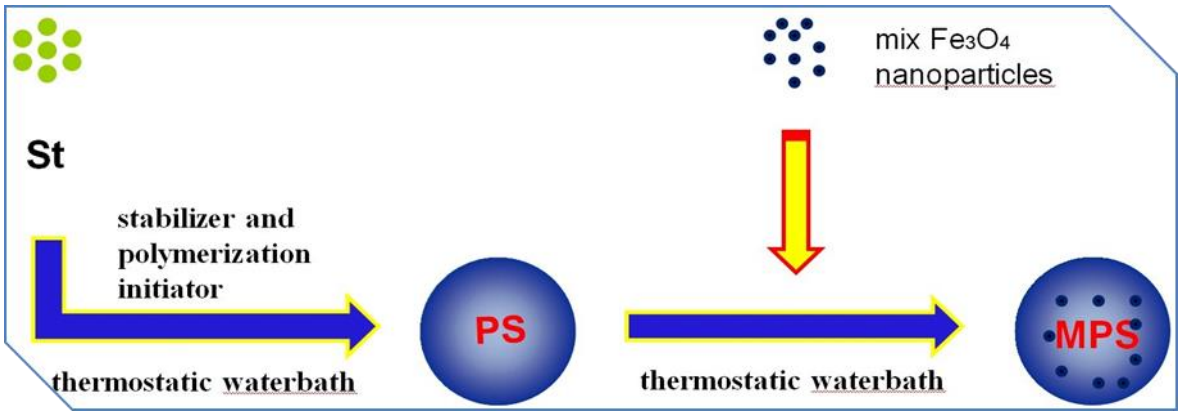
Keywords: Fe_3O_4 nanoparticles, magnetic polymer microspheres, immunomagnetic microspheres.

Based on the porous polystyrene microspheres, submicron polystyrene magnetic microspheres have been synthesized by using Fe_3O_4 nanoparticles with different surface modifications as magnetic material. Further magnetic separation experiments by using the immune magnetic macrospheres coated with salmonella specific antibodies showed highly separation efficiency on salmonella samples. Firstly, by using $Fe(acac)_3$ (iron acetylacetonate) as metal organic precursor, PEG, PVP and PVP/triethylene glycol coated iron oxide nanoparticles have been synthesized through the thermal decomposition method respectively. The magnetic property of the above three magnetic nanoparticles was analyzed. The results showed that the PVP/triethylene glycol coated iron oxide nanoparticles were characterized by the highest saturation magnetization intensity, which is more suitable to be used for preparation of magnetic microspheres than the others.

Secondly, monodisperse magnetic polystyrene microspheres have been successfully synthesized by adding the iron oxide nanoparticles into the dispersion polymerization reaction system of preparing porous polystyrene microspheres. PVP and PVP/triethylene glycol-coated iron oxide nanoparticles were respectively used for the preparation. The magnetic property and colloid stability of acquired magnetic polystyrene microspheres were analyzed. The results showed that magnetic polystyrene microspheres by using PVP/triethylene glycol-coated iron oxide nanoparticles as materials were characterized by better magnetic response, which is more suitable for the preparation of immunomagnetic microspheres.

Finally, through the electrostatic interaction between magnetic beads andanti-Salmonella CSA-1 antibody，submicro immunomagnetic beads were prepared and applied in separating Salmonella sp.



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P-08

Amphiphilic dendrimer delivering BCL-3 siRNA for potent nasopharyngeal carcinoma therapy

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Keywords: BCL-3 gene, nasopharyngeal carcinoma, amphiphilic dendrimer, siRNA delivery

OBJECTIVE The present study examined the potential of amphiphilic dendrimer mediated BCL-3 siRNA delivery in treating nasopharyngeal carcinoma. **METHODS** BCL-3 siRNA and amphiphilic dendriplexes were formed and characterized by RNase A protection assay. The knockdown efficiency at different concentration and N/P ratio in C666-1 cells were evaluated by PCR. The anti-tumor effect were investigated in C666-1 xenografts and patients' xenografts respectively. **RESULTS** In this study, we show for the first time that the amphiphilic dendrimer can form stable dendriplexes with BCL-3 siRNA and serve as siRNA carriers. Amphiphilic dendrimer can protect BCL-3 siRNA from RNase A digestion for as long as 30 min at an N/P ratio of 5 and effective knockdown BCL-3 gene expression in C666-1 cells at an optimum condition of N/P ration of 5 at 10 nM. We also studied the anti-tumor effect of BCL-3 siRNA dendriplexes in C666-1 tumors and primary tumors xeno-2117. The BCL-3 siRNA dendriplexes can effectively inhibit tumor growth without obvious toxicity. **CONCLUSION** The results demonstrated that amphiphilic dendrimers were very suitable as siRNA nanocarriers with effective gene knockdown efficiency. What's more, BCL-3 could be a very promising therapy target and BCL-3 siRNA dendriplexes could be a potent nanomedicine for nasopharyngeal treatment.

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Magnetic materials based electrochemiluminescence immunoassay using home-made detecting cell

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Keywords: Magnetic materials; Electrochemiluminescence; Graphite-like carbon nitride; Carbon nannospheres; Carcinoembryonic antigen

Due to their attractive electrical and optical characteristics, nanomaterials have been used to facilitate the immobilization of biomolecules and improve electrochemical properties of the transducer or as carriars of labels [1-3]. Further improvements in sensitivity and reproducibility will extend practical applications of the nanomaterials based detection platforms to wider range of problems [4]. In this study, Fe_3O_4 functionalized graphene with magnetic property were prepared and applied in the immobilization of biomolecules owing to its advantages: (1) more specific surface area obtained for the binding of larger amounts of biomolecules; (2) lower mass transfer resistance; (3) selective separation of the immobilized biomolecules from a reaction mixture on application of a magnetic field. Using prepared graphite-like carbon nitride quantum dots functionalized carbon nanospheres as labels for signal amplification, a novel electrochemiluminescence immunosensor for sensitive detection of carcinoembryonic antigen was constructed, which was assembled on the surface of indium tin oxide glass. The analyte was detected in a home-made flow injection electrochemiluminescence cell through the immunosensor. With the aid of a magnet, the prepared immunosensor could be easily separated and collected. Under optimal conditions, a wide detection range and low detection limit were achieved. In particular, this approach presents a novel class of combining bifunctional nanomaterials with preferable electrochemiluminescence properties and excellent magnetism, which provides a new promising platform for clinical immunoassays of other biomolecules.

Acknowledgements

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P-10

Self-carried curcumin nanoparticles for in vitro and in vivo cancer therapy with real-time monitoring of drug release

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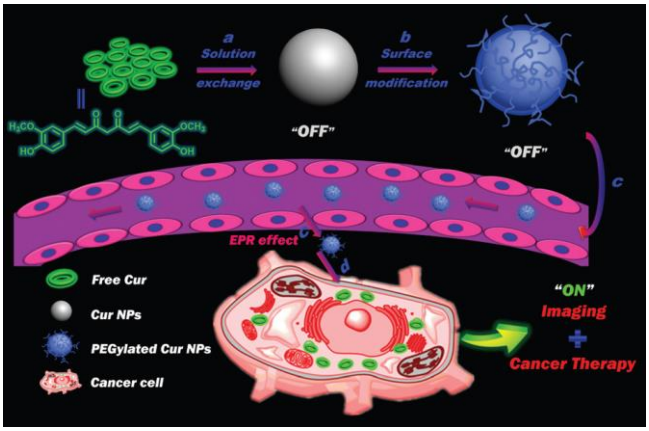
Keywords: 5 keywords maximum related to your abstract**.**

The use of different nanocarriers for delivering hydrophobic pharmaceutical agents to tumor sites has garnered major attention. Despite the merits of these nanocarriers, further studies are needed to improve their drug loading capacities (which are typically <10%) and reduce their potential systemic toxicity. Therefore, the development of alternative self-carried nanodrug delivery strategies without using inert carriers is highly desirable. In this study, we developed a self-carried curcumin (Cur) nanodrug for highly effective cancer therapy in vitro and in vivo with real-time monitoring of drug release. With a biocompatible C18PMH-PEG functionalization, the Cur nanoparticles (NPs) showed excellent dispersibility and outstanding stability in physiological environments with drug loading capacities >78 wt%. Both confocal microscopy and flow cytometry confirmed the cellular fluorescence "OFF–ON" activation and real-time monitoring of the Cur molecule release. In vitro and in vivo experiments clearly show that the therapeutic efficacy of the PEGylated Cur NPs is considerably better than that of free Cur. This self-carried strategy with real-time monitoring of drug release may open a new way for simultaneous cancer therapy and monitoring.



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Ultrasensitive electrochemiluminescence sensor for detection of mercury ion on portable paper-based device

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Keywords: Electrochemiluminescence; Paper-based device; Mercury ion; Carbon dots

Paper, as a ubiquitous material in everyday life, has recently emerged as flexible substrates for the development of paper-based microfluidic devices that are created by patterning hydrophobic materials in hydrophilic paper [1-3]. It offers advantages of low cost, ease of fabrication, good printability, high flexibility, and light weight. They are considered to be the ideal bioassay platforms to develop point-of-care diagnostic devices for use in less-industrialized countries, in remote settings, or even in home care services [4,5]. In this work, a portable paper-based analytical device has been proposed for electrochemiluminescence detection of mercury ion based on oligonucleotide. The functionalized wax-patterned three-dimensional paper-based electrochemiluminescence device that can provide fast, cost-effective, simple, and sensitive detection for analysis was dependent on Hg^{2+} induced conformational change of DNA strands through the formation of T-Hg^{2+}-T complex. Using carbon dots functionalized SiO_2 nanosphere as signal amplification, excellent electrochemiluminescence performance was exhibited through a sandwich-type immunoassay. This simple and cost effective assay was successfully applied to detect Hg^{2+} in lake water and human serum samples. These characteristics suggested that this device could provide quantitative information very conveniently and show great potential to broad fields of resource-limited analysis, medical diagnostics, and on-site environmental detection. In brief, combining the potential advantages of feasible, easy transportation, and manipulation with cheap price, this device will also could be applied to obtain quantitative data from the fields of on-site detection, medical diagnostics, and environmental pollution evaluation.

Acknowledgements

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P-12

Synthesis of g-C_3N_4 nanodot-based silica gels for white-light-emitting devices

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Keywords: White LED, metal free, g-C_3N_4, silica gel

A facile approach is developed to fabricate graphite carbon nitride (g-C_3N_4) nanodot-based metal-free white light emitting diodes (WLED) with strong fluorescence, excellent bio-compatibility, low-cost, and flexible properties. The material is fabricated by first synthesizing g-C_3N_4 nanodots using a simply one-step solid-phase thermal process, followed by convenient surface functionalization by N-(β-aminoethyl)-γ-aminopropylmethyldimethoxysilane to form a novel type of flexible nanocomposite of g-C_3N_4 nanodot/silica gel (g-CNDs-gel). The fabricated g-CNDs-gel can be uniformly coated onto a UV-LED bulb (peak wavelength at 365 nm) by simple dip-coating, enabling a novel type of metal-free WLED that is of high quantum yield (27%), good biocompatibility, and low-cost. The g-CNDs-gels reported here hold great promise in biocompatible devices that is amenable to large-scale production.

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The Biological Application of Rare Earth Upconversion Luminescence Nanoparticles

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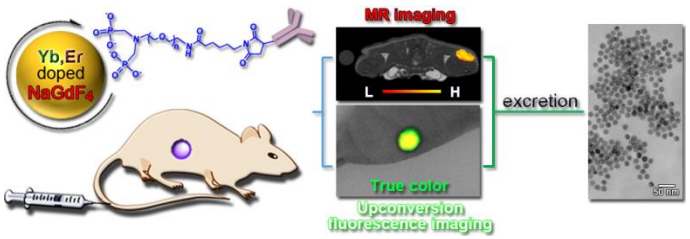
Keywords: upconversion luminescence, molecular imaging, nanoprobe, tumor detection.

Owing to the unusual magnetic and optical properties associated with f-electrons, rare-earth elements are very suitable for creating functional materials potentially useful for tumor imaging[1-3]. Nanometer-sized particle offers such a platform that versatile unique properties of the rare earth elements can be integrated, yet the development of rare-earth nanoparticle-based tumor probes suitable for imaging tiny tumors *in vivo* remains difficult, which challenges not only the physical properties of the nanoparticles but also the rationality of the probe design.

Here we talk about the size control synthesis, property studies, biodistribution of magnetic/upconversion luminescence (UCL) nanoparticles together with their applications in tumor imaging. We first prepared $NaGdF_4$:Yb,Er magnetic/upconversion luminescence nanoparticles, and the PEGylated nanoparticles were used to achieve a MRI/UCL dual-modality molecular probe. Owing to the excellent properties of the molecular probes, tumors smaller than 2 mm was successfully imaged *in vivo*. Then, in order to obtain nanoprobe with higher luminescence efficiency, the core-shell architecture $NaGdF_4$:Yb,Er@$NaGdF_4$ nanoparticles were prepared. A primary colorectal tumor was built in rodents through the induction of 1,2-dimethylhydrazine. The UCL nanprobes are favorable for excluding the interference of autofluorescence from tissues and strong fluorescence signal from ingested foods, and the early detection of primary tumor was successfully achieved. The current biological study based on UCL nanoparticles paves a novel strategy to improve the sensitivity of tumor imaging.



Schematic drawing of the dual-modality imaging of tumor based on the UCL nanoparticles and the clearance behavior.

References:

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P-14

Carbon dot-based fluorescence turn-on sensor for hydrogen peroxide with a photo-induced electron transfer mechanism

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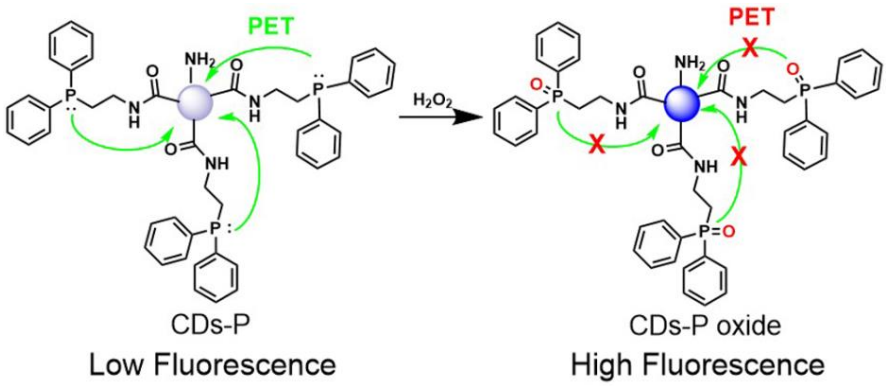
Keywords: Carbon dots, photo-induced electron transfer, fluorescent sensor, hydrogen peroxide



Hydrogen peroxide (H_2O_2) is a major reactive oxygen species (ROS) in living organisms. Recent studies have demonstrated that H_2O_2 poses a substantial threat to living cells when its concentration exceeds 0.7 μM. An abnormal level of H_2O_2 in the biological system is an indicator of health issues. H_2O_2 is also extensively applied in chemical fields, biological fields, food and environmental disinfection, and so on. High H_2O_2 concentration could be a great threat to the environment and human health; for example, it may lead to the generation of acid rain and could induce a number of diseases, including Parkinson's disease, senile dementia, and even cancer. Obviously, sensitive and reliable detection of H_2O_2 is of particular importance in biological and toxicological diagnosis.

Here we reported a carbon dot-based fluorescence turn-on sensor (CDs-P) based on photo-induced electron transfer (PET) mechanism for the detection of H_2O_2 in aqueous solution. For this sensor, diphenylphosphine moiety and carbon dots (CDs) were served as the PET donor and acceptor, respectively. The PET process of CDs-P can be effective cancelled by the formation of CDs-P oxide after selectively reacting with H_2O_2. CDs-P shows good sensing performance for H_2O_2 in a wide pH range from 4 to 12, with a linear range of detection from 0 to 2 μM and detection limit of 84 nM. The sensing procedure is through a specific chemical reaction, which enables its rapid response (40 s) and excellent selectivity toward H_2O_2. The synthesis approach of the sensor is also more cost-effective and co-friend as compared to those applied for synthesizing other fluorescent materials, such as organic dyes, noble metal nanoparticles and semiconductor QDs.

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A pH-sensitive micelle based on poly(ethylene glycol)-b-poly(L-lysine) copolymer for anticancer drug delivery

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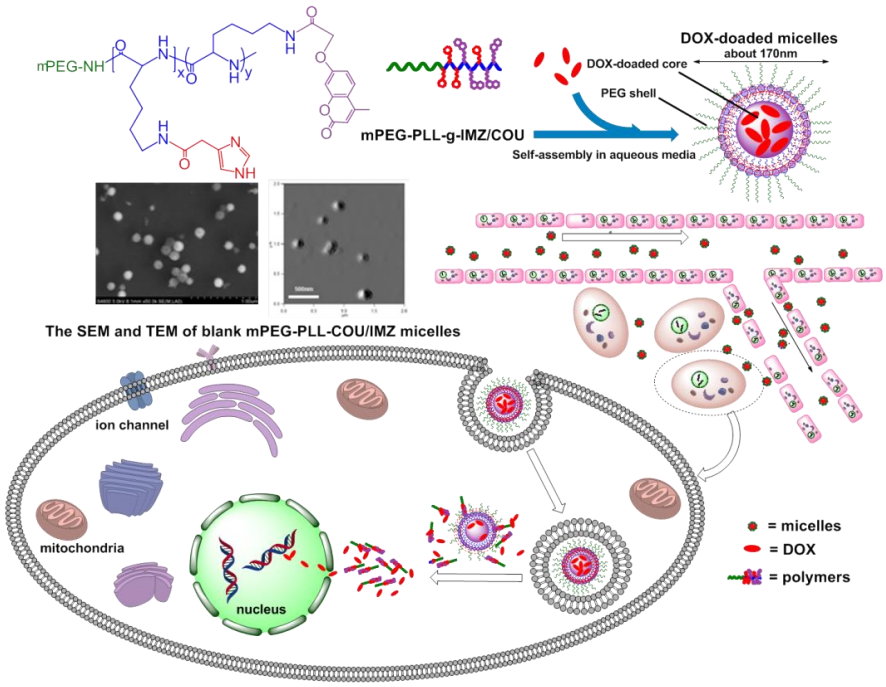
Keywords: pH-Sensitive, imidazole, poly(L-lysine), anticancer drug delivery

New anti-tumor drug delivery vectors with stimuli responsivity and biodegradability are desirable in recent decades[1]. Herein, a polymeric micelle with imidazole and coumarin derivative grafted on poly(ethylene glycol)-b-poly(L-lysine) (mPEG-PLL-g-COU/IMZ) copolymer was prepared with very low critical micelle concentration (CMC, 9.49×10^{-6}mol/L) . Anticancer drug doxorubicin (DOX) was encapsulated in the micelles. The release profile, hydrodynamic diameter, PDI and zeta potential of DOX-loaded micelles in different pH values were investigated. The polymeric micelles exhibited high drug-loading content(DLC, 17.2%) and encapsulation efficiency(EE, 50.5%) due to π-π stacking interaction between DOX and coumarin derivatives[2]. The morphology of blank and DOX loaded micelles was investigated by atomic force microscope (AFM) and scanning electron microscope (SEM). The murine breast carcinoma cells 4T1 were incubated with drug-loaded micelles to study the cellular uptake and anti-cancer effect in vitro. The flow cytometry and laser scanning confocal microscope (CLSM) results revealed that the mPEG-PLL-g-COU/IMZ copolymer micelles showed high cellular uptake capability and in vitro anticancer activity. This study suggested the mPEG-PLL-g-COU/IMZ copolymer was a promising alternative in microenviroment induced drug delivery system toward tumors.



Scheme 1. Schematic illustration of self-assembly DOX-loaded micelles and subsequent intracellular DOX release.

Acknowledgement: National Science Foundation of China (NSFC, No. 31170921, 51133004)

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P-16

Graphitic Carbon Nitride Nanosheet @ Metal-Organic Framework Core-shell Nanoparticles for Photo-chemo Combination Therapy

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Keywords: Carbon nitride, Combination therapy, Drug delivery, Nanoscale metal-organic frameworks, Core-shell nanoplatform.

Recently, nanoscale metal-organic frameworks (NMOFs) start to be developed as a promising platform for bioimaging and drug delivery, which combine many potent features such as high loading capacity, progressive biodegradability and low cytotoxicity. On the other hand, combinational therapies using multiple approaches are demonstrated to achieve much enhanced efficacy. Herein, we report, for the first time, core-shell nanoparticles consisting of a photodynamic therapeutic (PDT) agent and MOF shell while simultaneously carrying chemotherapeutics drug for effective combinational therapy. In the work, core-shell nanoparticles of zeolitic-imadazolate framework-8 (ZIF-8) as shell embedded with graphitic carbon nitride (g-C_3N_4) nanosheets as core are fabricated by growing ZIF-8 in the presence of g-C_3N_4 nanosheets. Doxorubicin hydrochloride (DOX) is then loaded into the ZIF-8 shell of the core-shell nanoparticles. The combination of the chemotherapeutic effects of DOX and the PDT effect of g-C_3N_4 nanosheets can lead to considerably enhanced efficacy. Furthermore, the red fluorescence of DOX and the blue fluorescence of g-C_3N_4 nanosheets provide additional function of dual-color imaging for monitoring the drug release process.

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P-17

A pH-Controlled Nitric Oxide-Generating Hollow Microsphere System for Overcoming P-Glycoprotein-Mediated Multidrug Resistance for Cancer Therapy

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Keywords: Nitric oxide, drug release, P-glycoprotein, multidrug resistance

Multidrug resistance (MDR) resulting from the overexpression of drug transporters such as P-glycoprotein (Pgp) increases the efflux of drugs and thereby limits the effectiveness of chemotherapy. To address this issue, this work develops an injectable hollow microsphere (HM) system that carries the anticancer agent irinotecan (CPT-11) and a nitric oxide (NO) releasing donor (NONOate). Upon injection of this system into acidic tumor tissue, environmental protons infiltrate the shell of the HMs and react with their encapsulated NONOate to form NO bubbles that trigger localized drug release and serve as a Pgp-mediated MDR reversal agent. The site-specific drug release and the NO-reduced Pgp-mediated transport can cause the intracellular accumulation of the drug at a concentration that exceeds the cell-killing threshold, eventually inducing its antitumor activity. These results reveal that this pH-responsive HM carrier system provides a potentially effective method for treating cancers that develop MDR.

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P-18

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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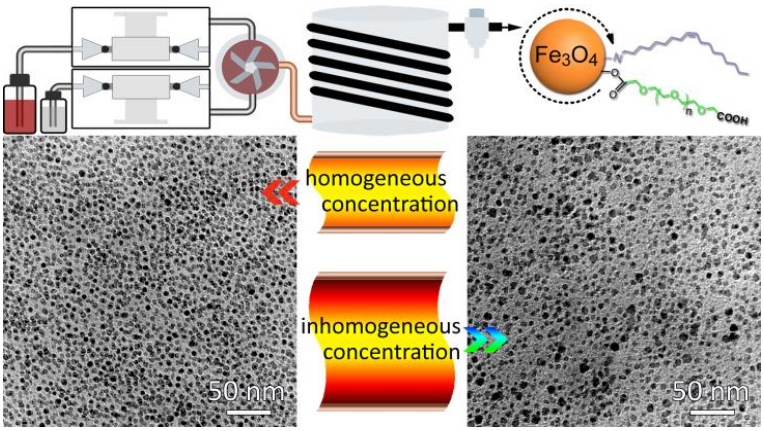
Keywords: flow synthesis, PEGylated Fe_3O_4 nanoparticle, particle size distribution, flow parameters.

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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Multifunctional magnetic hydrogel with controllable magnetothermal effect in alternating magnetic field

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Keywords: magnetic hydrogel; magnetothermal effect; controlled release;

Heat can be used as effective treatment means. Moderate temperature is suitable for alleviating inflammation, but temperature for eradicating cancer cell is relatively higher. Since different heat temperatures are needed in certain stages of treatment in clinic, it's significant to kill two or more birds with one stone. Induction heat treatment based on alternating magnetic field draws increasingly attention for its various advantages. However, it's inconvenient to tune the heat generation in practice when the generator of alternating magnetic field is designed to output energy at rated power. In this work, we propose a novel magnetic hydrogel oriented by magnetic field as a solution. By tuning the relative angle between aligned magnetic colloidal assemblies embedded magnetic hydrogel and applied alternating magnetic field, we can conveniently control the heat generation to switch between different functions. The controllable magnetothermal effect can also be used as trigger of drug controlled release.

This findings have been published on Advanced Materials: 2015,27(15):2507-14

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P-20

Interrogation of Cellular Innate Immunity by Diamond-NanoneedleAssisted Intracellular Molecular Fishing

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Keywords: Diamond nanoneedles, intracellular sensing, in situ detection, innate immunity, STING activation**.**

Understanding intracellular signaling cascades and network is one of the core topics in modern biology. Novel tools based on nanotechnologies have enabled probing and analyzing intracellular signaling with unprecedented sensitivity and specificity. In this study, we developed a minimally invasive method for in situ probing specific signaling components of cellular innate immunity in living cells. The technique was based on diamond-nanoneedle arrays functionalized with aptamer-based molecular sensors, which were inserted into cytoplasmic domain using a centrifugation controlled process to capture molecular targets. Simultaneously, these diamond-nanoneedles also facilitated the delivery of double-strand DNAs (dsDNA90) into cells to activate the pathway involving the stimulator of interferon genes (STING). We showed that the nanoneedle-based biosensors can be successfully utilized to isolate transcriptional factor, NF-κB, from intracellular regions without damaging the cells, upon STING activation. By using a reversible protocol and repeated probing in living cells (**Fig 1**), we were able to examine the singling dynamics of NF-κB, which was quickly translocated from cytoplasm to nucleus region within ~ 40 min of intracellular introduction of dsDNA90 for both A549 and neuron cells. These results demonstrated a novel and versatile tool for targeted in situ dissection of intracellular signaling, providing the potential to resolve new sights into various cellular processes.

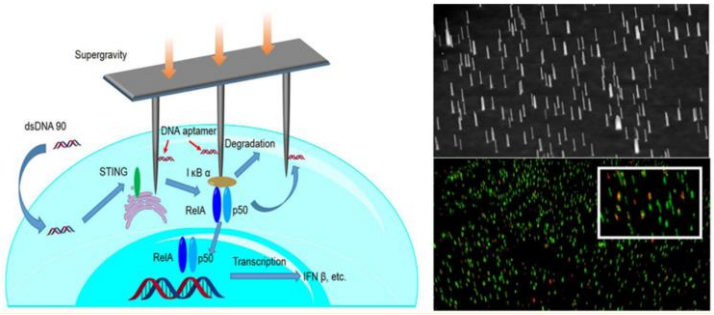

Figure 1. Illustration of the intracellular molecular fishing and representative result.

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Reference:

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

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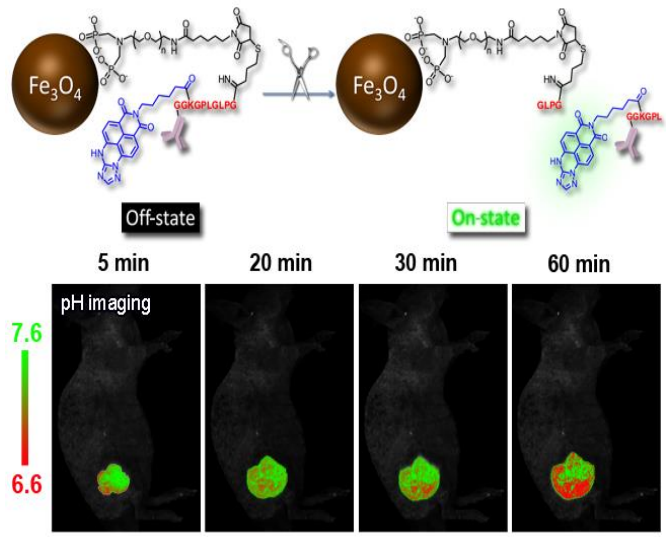
Keywords: Fe_3O_4 nanocrystals, protease-activated, pH mapping, ratiometric fluorescence, smart probe**.**

Tumor microenvironment is strongly correlated with prognostic factors relating to growth, invasion, and metastasis of malignant tumors.[1-3] 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.



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.[4]

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P-22

Flexible and Highly Reproducible Printed Surface Enhanced Raman Spectroscopy Substrates for the Detection of Chemicals and Drugs

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Keywords: Surface enhanced Raman spectroscopy; Screen Printing; Food safety; Amoxicillin**.**

Surface enhanced Raman spectroscopy (SERS) is a powerful vibrational spectroscopy technique that allows for highly sensitive structural detection of low-concentration analytes via the amplification of electromagnetic fields generated through the excitation of localized surface plasmon resonances of the substrate. The current fabrication methods for SERS substrates are often complex and time-consuming. As a competitive alternative, the development of simple, facile and low-cost methods are becoming increasingly important. Printing technology is a strong candidate for high throughput, facile and cost-effective fabrication of large-scale orderly functional patterns or arrays. And hence, we used the screen printing-assisted growth method to prepare the patterned ZnO nanowires arrays, which shows both hydrophilicity and lipophilicity properties. Furthermore, after coating Ag NPs on the patterned nanowires arrays, we have developed an ultra-sensitive three-dimension SERS substrate. The detection limit of Malachite green of the as-prepared ZnO nanowires arrays is as low as 10^{-12} M, while the analytical enhancement factor is about 2.5×10^{10}. Combined with the sensitivity and uniformity, the Ag NPs decorated ZnO nanowires arrays is applied for the quick detection of low concentrations of molecules related to food safety, such as melamine and amoxicillin.

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Low-Cost Graphene Quantum Dots with Peroxidase Catalytic Activity

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Keywords: Graphene quantum dots(GQDs), peroxidase-like activity.

Graphene quantum dots (GQDs) is a type of zero-dimensional material with characteristics derived from both grapheme oxide (GO) and carbon dots (CDs). GQDs exhibit a higher peroxidase-like activity than GO, which can catalyze the oxidation of many substrates, such as 3,3,5,5-tetramethylbenzidine (TMB), in the presence of H_2O_2.[1]

In this manuscript, we report a facile one-step synthesis of GQDs by acidic treatment of carbon fibers (cf), graphite (g) and *N*-doped grapheme(*N*-G) as raw materials. cf-GQDs, g-GQDs and *N*-GQDs were produced in high yield and their peroxidase catalytic avtivities were investigated. It was found that g-GQDs and *N*-GQDs exhibited excellent peroxidase-like activity, although g-GQDs was prepared from low cost graphite. These GQDs have been further used in glucose determination in buffer solution or diluted blood and fruit juice samples.

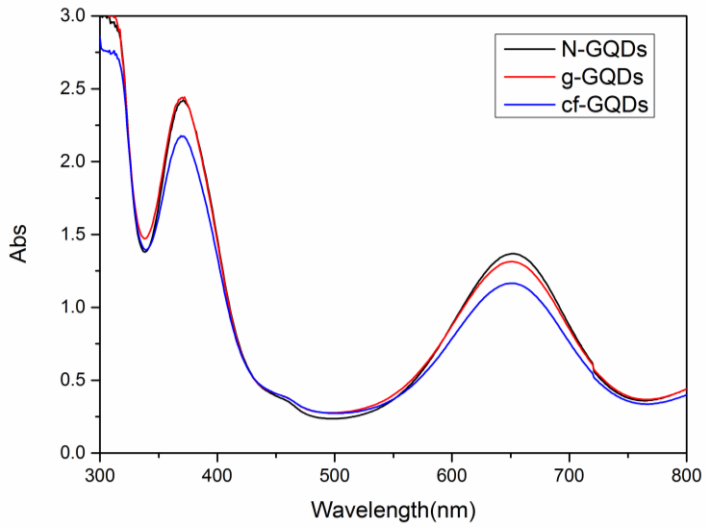

Fig. 1 The UV-Vis absorption spectra of M+ TMB + H_2O_2 at 35 ℃ after 5 min (M was *N*-GQDs, g-GQDs or cf-GQDs) in PBS (pH=4). The concentration of M , TMB, and H_2O_2 are 40 μg • mL^{-1}, 800 μmol • L^{-1} and 50 mmol • L^{-1} respectively.

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P-24

Diamond nanoneedle arrays for enhanced delivery of drug molecules to different cell lines

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Keywords: intracellular delivery; nanoneedle arrays; diamond nanoneedles; drug delivery; drug resistance

Abstract

Nanotechnologies for intracellular delivery are of great value in clinical and biological research. Diamond nanoneedle arrays are a novel and attractive platform to facilitate drug delivery with minimal toxicity. Using our technique, the cellular membranes can be temporarily disrupted for enhanced diffusion of drug molecules to cytoplasm. Here we show that this technique is applicable to deliver different types of anticancer drugs into a variety of cell lines, although the membrane of each cell line possesses varied rigidity and hardness and each drug has its own unique targets. When anticancer drugs and nanoneedle arrays are used together to treat cancer cells cell viability dramatically decreases up to 40% in comparison with the cells treated with the drugs only. More attractively, for the first time to the best of our knowledge, we use this typr of technique to conquer drug resistant issue. Therapeutic molecules were delivered to drug resistant cells by nanoneedle arrays, resulting in the significant decrease of cell viability, the cells only treated with the same concentration of drug are essentially not affected due to the resistance. These results indicated that nanoneedle arrays represent an effective approach to enhace the anticancer efficacy of different types of chemotherapeutics and to reduce the drug resistance issue. Such approach may also benefit to clinical applications.

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Investigation of biological cell–small molecular interactions based on gold film SPR sensor using a LSCI–SPR

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Keywords: interaction; biological cell–small molecular; LSCI-SPR.

Folic acid is essential for DNA synthesis, amino acid interconversion, methylation and, retntial cell growth. Du to the existing pre-neoplastic and neoplastic lesions in animals, folic acid upplementation increases the tumor burden and there are folic acid receptor proteins on the surface of the cell in different amount [1]. Many researchers have invested the affect cueing cancer medicine by labeled and free labeled method [2]. We used a laser scanning confocal imaging–surface plasmon resonance system (LSCI–SPR) based on an angle modulating surface plasmon resonance system to investigate the interaction between folic acid and the biological cell thorough the interaction of folic acid and foliate receptor and estimate the binding rate for adherent and suspended cells. There are good linear relationship between the SPR peak changes and the cell concentrations, and the fluorescent imagine give the further perfect identify datum. The detection limit is as low as 1.0×103 cells/mL and the linear coefficients were over 0.95200 for Mouse lymphoma (L5178Y) cells, mouse lymphoma (EL4) cells, Mouse Tlymphocytes (Cl.Ly) cells, human lung cancer (A549) and Human oral epidermis carcinoma cells (KB).The results show that the FAR express on the KB cell is higher than that of the A549 cell, which is similar to the previous work on adherent cells. It is the first time to investigate the interaction of the suspended cell with the small molecular using LSCI–SPR system. The results indicate that SPR method has the potential future application in analyzing the affinity of the small molecular and biology cell in free labeled and can get the quantitative parameter. At the same time, the results can distinguish the expression level of the suspension cell with the similar to that in adherent and suspension cells.

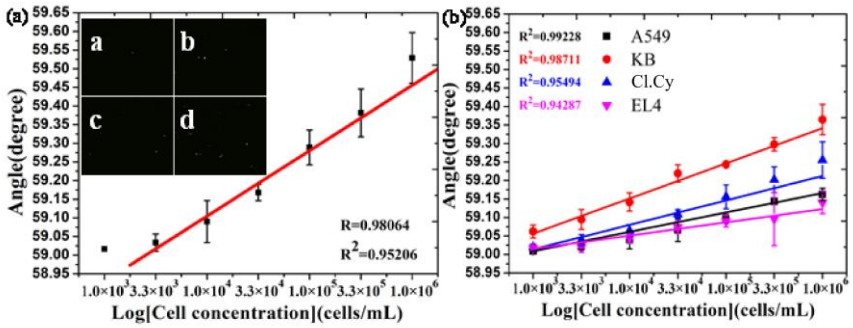

Fig.1. SPR response with the different concentrations of the cells changing from 1.0 × 103 cells/mL to 1.0 × 106 cells/mL in PBS buffer: (a) SPR signal at different concentration of L5178Y cell and fluorescence images obtained from the covering of the L5178Y cells by interaction with folic acid that self-assembled on the gold film at different concentrations in PBS solution (Insert graphs with letters a, b, c, and d show the condition of L5178Y cells at 1.0×103, 1.0×104, 1.0×105, and 1.0×106 cells/mL concentrations interact with FA modified on the chip surface); (b) SPR signal for A549, KB, Cl.Cy and EL4 cell. The error bars represent the standard deviations taken from at least three independent measurements.

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One-Step Reaction for Fluorescent Silicon Nanorods

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Keywords: Silicon, Synthesis, Fluorescent, Nanorods

Silicon (Si) is the most widely used semiconductors in commercial electronic and optoelectronic devices, but it is poor light emitters and weak light absorbers due to their indirect band gaps. Si quantum dots, however, can exhibit very bright visible-light emission with size-tunable color and a variety of synthetic methods have been developed for Si nanocrystals. Quantum rods of Si also luminescence, and like other semiconductor nanorods, should exhibit an even wider range of unique optical properties, such as enhanced birefringence, faster carrier relaxation, and higher photon absorption cross sections, but their synthesis is much less developed. This study represents the first synthesis of silicon nanorods using polyols-mediate process, and it illustrates the potential for this nanorods as cellular imaging probe.

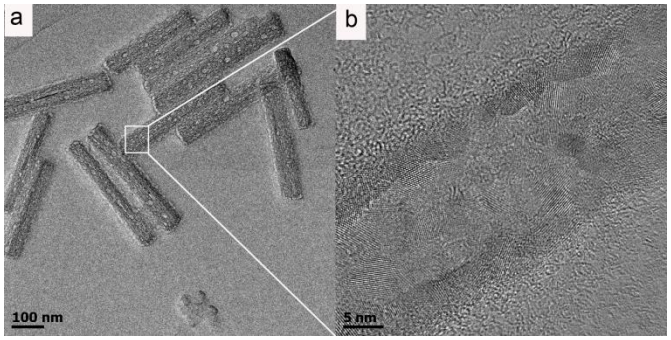

Figure1: (a)TEM, and (b) HRTEM images of the obtained silicon nanorods.

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Mono-disperse Silver Quantum Dots Modified Formvar Films

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Ion implantation, as an efficient approach to dope semiconductor materials, is an important surface modification technique for electronic industry.1, 2 Implantation with different ions can change the photo-, electronic-, and magnetic- properties of the host materials.3, 4 So far, most reports on ion implantation have focused on semiconducting and metal materials, less effort has been contributed to organic film target, especially for organic functional materials. In this work, formvar films were treated with silver (Ag) ion implantation with different doses.5 Interestingly, it was found that the implanted Ag ions form Ag quantum dots (AgQDs) which present uniform distribution in the formvar films. The density of AgQDs has a significant increase as the implantation dose increases, while the lateral size range of AgQDs becomes similar (~3- 4 nm). In addition, bacteria culture tests show that the formvar film implanted with AgQDs can effective kill escherichia on the films. The same implantation approach can also be extended for application in other matrix such as ZnS nanoribbon. It is expected that this approach may show huge potential for application in controlling diseases spreading via contact.

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Notepapers

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