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Acta Pharmaceutica Sinica B

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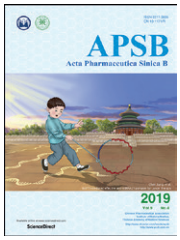
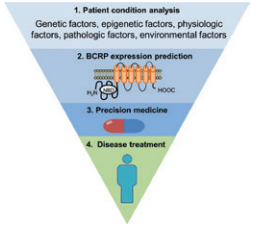


Graphical Abstracts/Acta Pharmaceutica Sinica B, 9 (2019) iii–viii

Reviews

Acta Pharmaceutica Sinica B, 9 (2019) 659

Development of precision medicine approaches based on inter-individual variability of BCRP/*ABCG2*



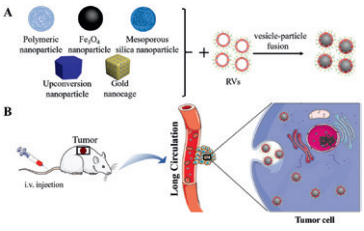
Liming Chen, Jose E. Manautou, Theodore P. Rasmussen, Xiao-bo Zhong

Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut, Storrs, CT 06269, USA

This review summarizes multiple factors, including genetic, epigenetic, physiologic, pathologic, and environmental factors, which have been reported to affect *ABCG2* expression or BCRP function. Understanding how these factors affect BCRP function is critical for the development of precision medicine approaches to achieve optimized therapeutic effects and minimize adverse effects when prescribing specific drugs to patients.

Acta Pharmaceutica Sinica B, 9 (2019) 675

Red blood cell membrane-camouflaged nanoparticles: a novel drug delivery system for antitumor application



Qing Xia, Yongtai Zhang, Zhe Li, Xuefeng Hou, Nianping Feng

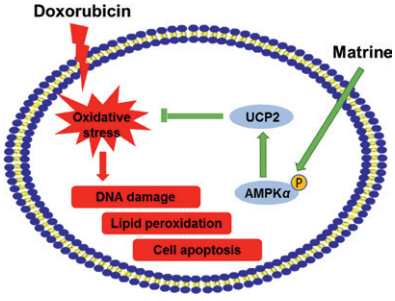
Department of Pharmaceutical Sciences, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China

In this review, the biomimetic platform of erythrocyte membrane-coated nano-cores is described with regard to coating mechanism, preparation methods, verification methods, and the latest anti-tumor applications. Finally, further functional modifications of the erythrocyte membranes and attempts to fuse the surface properties of multiple cell membranes are discussed.

Original articles

Acta Pharmaceutica Sinica B, 9 (2019) 690

Matrine attenuates oxidative stress and cardiomyocyte apoptosis in doxorubicin-induced cardiotoxicity *via* maintaining AMPK*α*/UCP2 pathway



Can Hu[a,b,c], Xin Zhang[a,b,c], Wenying Wei[a,b,c], Ning Zhang[a,b,c], Haiming Wu[a,b,c], Zhenguo Ma[a,b,c], Lingli Li[a,b,c], Wei Deng[a,b,c], Qizhu Tang[a,b,c]

[a]*Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan 430060, China*
[b]*Cardiovascular Research Institute of Wuhan University, Wuhan 430060, China*
[c]*Hubei Key Laboratory of Cardiology, Wuhan 430060, China*

Matrine attenuated oxidative stress and cardiomyocyte apoptosis in DOX-induced cardiotoxicity *via* maintaining AMPK*α*/UCP2 pathway, and it might be a promising therapeutic agent for the treatment of DOX-induced cardiotoxicity.

Acta Pharmaceutica Sinica B, 9 (2019) 702

Ablation of gut microbiota alleviates obesity-induced hepatic steatosis and glucose intolerance by modulating bile acid metabolism in hamsters

Lulu Sun[a], Yuanyuan Pang[a], Xuemei Wang[a], Qing Wu[a], Huiying Liu[a], Bo Liu[a], George Liu[b], Min Ye[c], Wei Kong[a], Changtao Jiang[a]

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[b]*Institute of Cardiovascular Sciences and Key Laboratory of Molecular Cardiovascular Sciences, Ministry of Education, Peking University, Beijing 100191, China*
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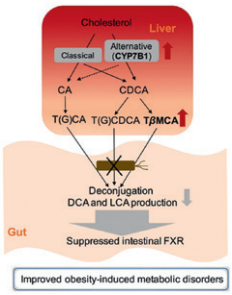

In the antibiotic-treated hamsters, hepatic CYP7B1-mediated alternative bile acid synthesis was activated. In hamsters, intestinal TβMCA accumulated and secondary bile acid levels were downregulated after gut microbiota depletion. Gut microbiota depletion-derived bile acid modulation results in intestinal FXR suppression and improvements of metabolic disorders in HFD-fed hamsters.

Acta Pharmaceutica Sinica B, 9 (2019) 711

Aspirin alleviates endothelial gap junction dysfunction through inhibition of NLRP3 inflammasome activation in LPS-induced vascular injury

Xing Zhou[a], Yanjiao Wu[a], Lifeng Ye[a], Yunting Wang[a], Kaimin Zhang[a], Lingjun Wang[d], Yi Huang[b], Lei Wang[a], Shaoxiang Xian[d], Yang Zhang[c], Yang Chen[a]

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[b]*Department of Stomatology, The First Affiliated Hospital, Jinan University, Guangzhou 510630, China*
[c]*Department of Pharmacological & Pharmaceutical Sciences, College of Pharmacy, University of Houston, Houston, TX 77204-5037, USA*
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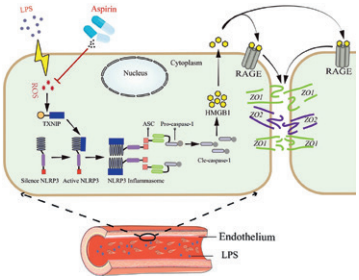


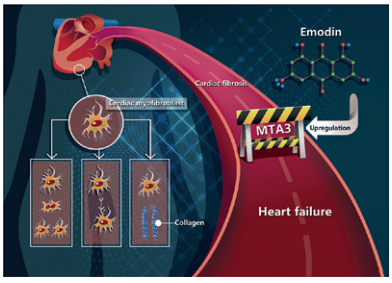
Aspirin inhibits the ROS–TXNIP signaling pathway to suppress NLRP3 inflammasome, thereby inhibits the activation of HMGB1–RAGE axis and eventually restores the tight junction proteins and permeability.

Acta Pharmaceutica Sinica B, 9 (2019) 724

Emodin alleviates cardiac fibrosis by suppressing activation of cardiac fibroblasts *via* upregulating metastasis associated protein 3

Dan Xiao[a], Yue Zhang[a], Rui Wang[a], Yujie Fu[a], Tong Zhou[b], Hongtao Diao[a], Zhixia Wang[a], Yuan Lin[a], Zhange Li[a], Lin Wen[a], Xujuan Kang[a], Philipp Kopylov[c], Dmitri Shchekochikhin[c], Yong Zhang[a,d], Baofeng Yang[a,e]

[a]*Department of Pharmacology (State-Province Key Laboratories of Biomedicine-Pharmaceutics of China, Key Laboratory of Cardiovascular Research, Ministry of Education), Harbin Medical University, Harbin 150081, China*
[b]*Department of Pharmacy, The First Affiliated Hospital of Harbin Medical University, Harbin 150081, China*
[c]*Department of Preventive and Emergency Cardiology, Sechenov First Moscow State Medical University, Moscow 119991, Russian Federation*
[d]*Institute of Metabolic Disease, Heilongjiang Academy of Medical Science, Harbin 150086, China*
[e]*Department of Pharmacology and Therapeutics, Melbourne School of Biomedical Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne 3010, Australia*



Emodin regulates cardiac fibrosis by metastasis associated protein 3 (MTA3). Cardiac fibroblast activation includes excess proliferation, migration and collagen synthesis, which eventually leads to heart failure. MTA3 is a key regulator of cardiac fibroblast activation, which is upregulated by emodin in the process of cardiac fibrotic inhibition.

Acta Pharmaceutica Sinica B, 9 (2019) 734

Cardamonin from a medicinal herb protects against LPS-induced septic shock by suppressing NLRP3 inflammasome

Zhilei Wang[a], Guang Xu[b], Yuan Gao[c], Xiaoyan Zhan[b], Nan Qin[b,d], Shubin Fu[b,d], Ruisheng Li[e], Ming Niu[b], Jiabo Wang[b], Youping Liu[a], Xiaohe Xiao[f], Zhaofang Bai[b,f]

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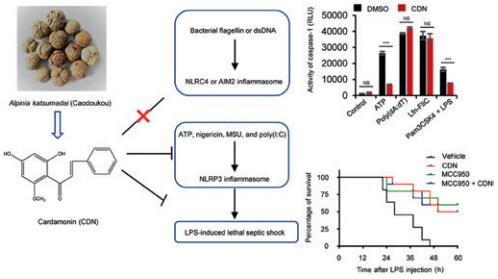


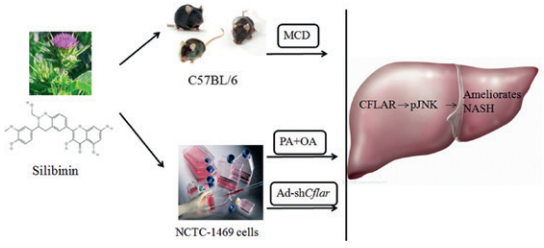
Cardamonin is a broad-spectrum inhibitor of NLRP3 inflammasome triggered by multiple stimuli. Moreover, the suppression of cardamonin on inflammasome activation is specific to NLRP3, not to NLRC4 or AIM2 inflammasome. Importantly, cardamonin improves the survival of mice suffering from LPS-induced lethal endotoxic shock, which is shown to be NLRP3 dependent.

Acta Pharmaceutica Sinica B, 9 (2019) 745

Silibinin ameliorates hepatic lipid accumulation and oxidative stress in mice with non-alcoholic steatohepatitis by regulating CFLAR-JNK pathway

Yayun Liu, Wei Xu, Ting Zhai, Jiaojiao You, Yong Chen

Hubei Province Key Laboratory of Biotechnology of Chinese Traditional Medicine, National & Local Joint Engineering Research Center of High-throughput Drug Screening Technology, Hubei University, Wuhan 430062, China



Silibinin could regulate CFLAR-JNK pathway to ameliorates hepatic lipid accumulation, insulin resistence and oxidative stress in C57BL/6 mice treated by methionine- and choline-deficient diet, and NCTC-1469 cells treated by the mixture of oleic acid and palmitic acid and adenovirus-down *Cflar*.

Acta Pharmaceutica Sinica B, 9 (2019) 758

Regulation of microbiota–GLP1 axis by sennoside A in diet-induced obese mice

Jiamei Le[a,b], Xiaoying Zhang[c], Weiping Jia[d], Yong Zhang[e], Juntao Luo[c], Yongning Sun[b,f], Jianping Ye[c,d,e]

[a]*Shanghai Key Laboratory of Molecular Imaging, Shanghai University of Medicine and Health Sciences, Shanghai 201318, China*
[b]*Department of Traditional Chinese Medicine, Shanghai Jiaotong University Affiliated Sixth People's Hospital, Shanghai 200233, China*
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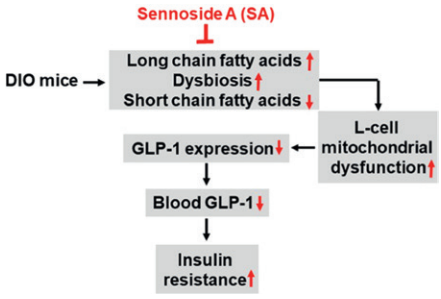

Sennoside A (SA) was found improving insulin sensitivity in diet-induced obesity mice through restoration of blood level of glucagon-like peptide 1. SA induced *Glp1* gene expression in L-cells of the colon tissue, which was associated with improvement of dysbiosis, short chain fatty acid abundance and mitochondrial function of L-cells.

Acta Pharmaceutica Sinica B, 9 (2019) 769

Up-regulation of glycolipid transfer protein by bicyclol causes spontaneous restriction of hepatitis C virus replication

Meng-Hao Huang[a], Hu Li[a], Rong Xue[b], Jianrui Li[a], Lihua Wang[b], Junjun Cheng[a], Zhouyi Wu[a], Wenjing Li[a], Jinhua Chen[a], Xiaoqin Lv[a], Qiang Li[c], Pei Lan[c], Limin Zhao[c], Yongfeng Yang[b], Zonggen Peng[a], Jiandong Jiang[a,c]

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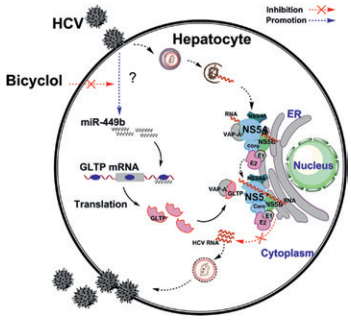
[b]*Department of Liver Diseases, the Second Hospital of Nanjing, Southeast University, Nanjing 210003, China*
[c]*State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100050, China*



Treatment of the HCV-infected Huh7.5 cells with bicyclol decreased the level of miR-449b and thus induced the expression of glycolipid transfer protein (GLTP). The up-regulated GLTP preferentially bound host cofactor vesicle-associated membrane protein-associated protein-A (VAP-A) in competition with the HCV NS5A, causing a decrease of the HCV replicative complex level of VAP-A/NS5A, and thus inhibited HCV replication.

Acta Pharmaceutica Sinica B, 9 (2019) 782

Chrysophanol protects against doxorubicin-induced cardiotoxicity by suppressing cellular PARylation

Jing Lu[a], Jingyan Li[a], Yuehuai Hu[a], Zhen Guo[a], Duanping Sun[b], Panxia Wang[a], Kaiteng Guo[a], Dayue Darrel Duan[c], Si Gao[d], Jianmin Jiang[a], Junjian Wang[a], Peiqing Liu[a]

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[c]*Laboratory of Cardiovascular Phenomics, Department of Pharmacology, University of Nevada Reno School of Medicine, Reno, NV 89557, USA*
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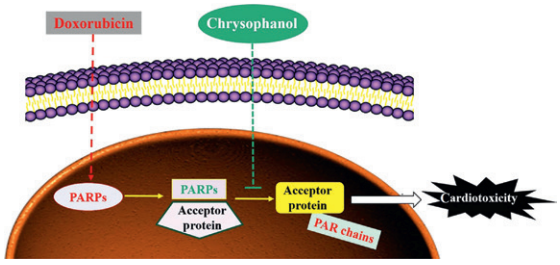


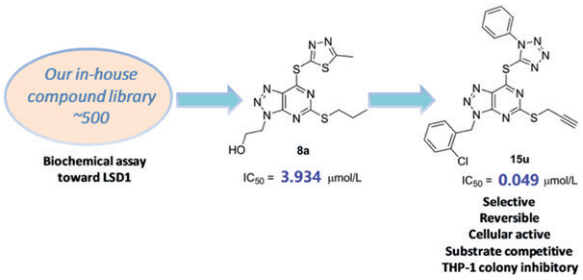
CHR protected against doxorubicin (DOX)-induced cardiomyocytes apoptosis, mitochondrial injury and heart dysfunction by suppressing cellular PARylation *in vitro* and *in vivo*.

Acta Pharmaceutica Sinica B, 9 (2019) 794

Development of the triazole-fused pyrimidine derivatives as highly potent and reversible inhibitors of histone lysine specific demethylase 1 (LSD1/KDM1A)

Zhonghua Li[a,c,d], Lina Ding[a,c,d], Zhongrui Li[a,c,d], Zhizheng Wang[a,c,d], Fengzhi Suo[a,c,d], Dandan Shen[a,c,d], Taoqian Zhao[a,c,d], Xudong Sun[a,c,d], Junwei Wang[a,c,d], Ying Liu[a,c,d], Liying Ma[a,c,d], Bing Zhao[a,c,d], Pengfei Geng[a,c,d], Bin Yu[a,b,c,d], Yichao Zheng[a,c,d], Hongmin Liu[a,c,d]

[a]*School of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou 450001, China*
[b]*State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing 210023, China*
[c]*Co-Innovation Center of Henan Province for New Drug R&D and Preclinical Safety, Zhengzhou 450001, China*
[d]*Key Laboratory of Advanced Drug Preparation Technologies, Ministry of Education of China, Zhengzhou 450001, China*



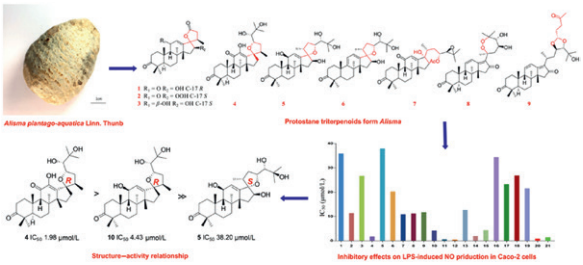
A series of triazole-pyrimidine derivatives were designed and synthesized as LSD1 inhibitors based on the hit compound **8a** from our in-house compound library. Among them, compound **15u** was identified as the most potent, selective and reversible LSD1 inhibitor, and also demonstrated excellent cellular inhibitory activities against AML cell lines.

Acta Pharmaceutica Sinica B, 9 (2019) 809

Novel C-17 spirost protostane-type triterpenoids from *Alisma plantago-aquatica* with anti-inflammatory activity in Caco-2 cells

Qinghao Jin[a], Jianqing Zhang[a,b], Jinjun Hou[a], Min Lei[a], Chen Liu[a], Xia Wang[a,c], Yong Huang[a], Shuai Yao[a], Bang Yeon Hwang[d], Wanying Wu[a,c], Dean Guo[a,b]

[a]*Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China*
[b]*School of Pharmacy, Shenyang Pharmaceutical University, Shenyang 110016, China*
[c]*University of Chinese Academy of Sciences, Beijing 100049, China*
[d]*College of Pharmacy, Chungbuk National University, Cheongju 2816, South Korea*



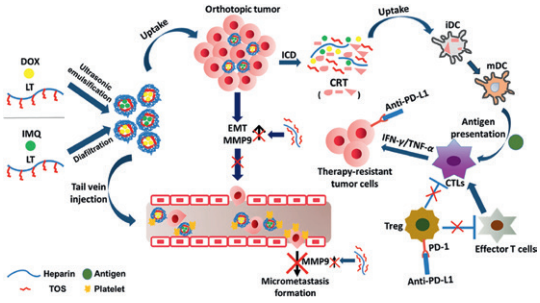
Nine novel compounds (**1–9**), were isolated from the of *Alisma plantago-aquatica* Linn. The isolated compounds proved to possess a very regular structure–activity relationship on inhibitory effects on LPS-induced NO production in Caco-2 cells.

Acta Pharmaceutica Sinica B, 9 (2019) 819

Multifunctional polymeric micelle-based chemo-immunotherapy with immune checkpoint blockade for efficient treatment of orthotopic and metastatic breast cancer

Jiaojie Wei, Yang Long, Rong Guo, Xinlei Liu, Xian Tang, Jingdong Rao, Sheng Yin, Zhirong Zhang, Man Li, Qin He

Key Laboratory of Drug Targeting and Drug Delivery Systems, West China School of Pharmacy, Sichuan University, Chengdu 610041, China



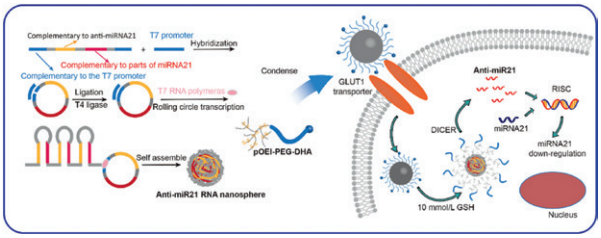
Chemotherapeutic doxorubicin (DOX) and immune adjuvant imiquimod (IMQ) were respectively encapsulated in LT micelles (LT-DOX/LT-IMQ) to initiate tumor apoptosis and anti-tumor immune response. However, the PD-L1/PD-1 axis impairs the T cell responses. Therefore, anti-PD-L1 was combined with LT-DOX/LT-IMQ to relieve the suppression and further promote the anti-tumor responses.

Acta Pharmaceutica Sinica B, 9 (2019) 832

GLUT1-mediated effective anti-miRNA21 pompon for cancer therapy

Qin Guo, Chao Li, Wenxi Zhou, Xinli Chen, Yu Zhang, Yifei Lu, Yujie Zhang, Qinjun Chen, Donghui Liang, Tao Sun, Chen Jiang

Key Laboratory of Smart Drug Delivery, Ministry of Education, State Key Laboratory of Medical Neurobiology, Department of Pharmaceutics, School of Pharmacy, Fudan University, Shanghai 201203, China



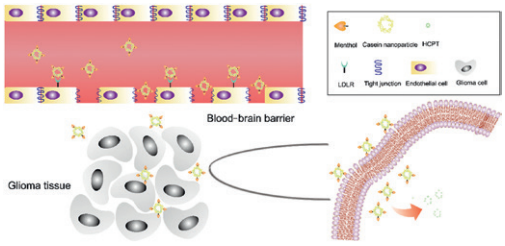
Preparation process, GLUT1-mediated transport and GSH-responsive drug release of DHA-targeting anti-miRNA21 nanopompons were reported. Nanopomponswere first obtained by rolling transformation transcription (RCT) and condensed by tumor-targteing pOEI-PEG-DHA.

Acta Pharmaceutica Sinica B, 9 (2019) 843

Menthol-modified casein nanoparticles loading 10-hydroxycamptothecin for glioma targeting therapy

Caifang Gao[a,b], Jianming Liang[a,c], Ying Zhu[c], Chengli Ling[d], Zhekang Cheng[e], Ruixiang Li[a], Jing Qin[a], Weigen Lu[b], Jianxin Wang[a]

[a]*Department of Pharmaceutics, School of Pharmacy, Fudan University & Key Laboratory of Smart Drug Delivery, Ministry of Education, Shanghai 201203, China*
[b]*Shanghai Institute of Pharmaceutical Industry, China State Institute of Pharmaceutical Industry, Shanghai 201203, China*
[c]*Guangzhou University of Chinese Medicine, Guangzhou 510006, China*
[d]*School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China*
[e]*School of Pharmacy, Minzu University of China, Beijing 100081, China*



Chemotherapy for the treatment of glioma remains to be unsatisfactory due to inefficient drug transport across the blood–brain barrier and insufficient accumulation in the tumor region. The prepared menthol-modified casein nanoparticles combined the advantages of traditional Chinese medicine strategy with modern drug delivery technology for brain tumor.

Acta Pharmaceutica Sinica B, 9 (2019) 858

Cholesterol-tuned liposomal membrane rigidity directs tumor penetration and anti-tumor effect

Hangyi Wu[a,b], Miaorong Yu[b], Yunqiu Miao[b], Shufang He[b], Zhuo Dai[b], Wenyi Song[b], Yuan Liu[b], Sha Song[b], Ejaj Ahmad[b], Dongkai Wang[a], Yong Gan[b]

[a]*Department of Pharmaceutics, Shenyang Pharmaceutical University, Shenyang 117004, China*
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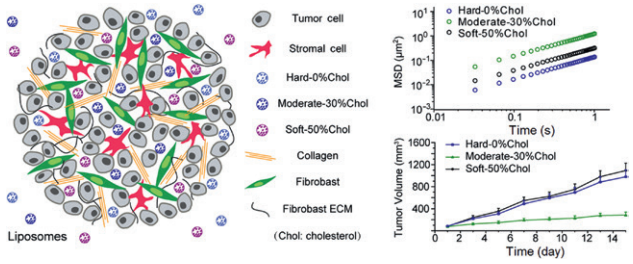

Liposomes with tunable rigidity were constructed conveniently by varying the contents of cholesterol. It is revealed that liposomes with moderate rigidity gained improved tumor penetration and enhanced anti-tumor effects compared to their soft and hard counterparts.

Acta Pharmaceutica Sinica B, 9 (2019)

Cover story

Front

Rolling cycle transcription (RCT) is an exquisite method to acquire quantity of therapeutic gene sequences. There is a similar rolling process between RCT and hoop rolling, a classic childhood game for Chinese children especially in old Peking. Just like RCT, favorable balance ability and coordination are demanded for stably maintaining the hoop rotation from falling down. For effective delivery of anti-miRNA21 sequences, a pompon-like nanoball is constructed through RCT. GSH-responsive cationic polymer polyethyleneimine (pOEI) was synthesized to protect the nanosphere from degradation and optimize the pompon-like nanoparticle to suitable size. Dehydroascorbic acid (DHA), which is a substrate of glucose transporter 1 (GLUT 1) and highly expressed on malignant tumor cells, was connected to pOEI through PEG, and then the polymer was used for contracting a RNA nanospheres into nanopompons. The anti-miR21 nanopompons showed its potential for effective cancer therapy.

Chen Jiang

Back

The cover story is drawn on the Chinese elemental “door god”. The door god and clouds represent bicyclol and glycolipid transfer protein (GLTP), respectively. The monsters that are attacking the cell or escaping represent hepatitis C virus (HCV). The door god coming with the clouds means that the expression of intracellular GLTP is increased after bicyclol treatment and thus the body's ability to resist viruses is enhanced, leading to the prevention of HCV from replication. The cover story tells a romance of how bicyclol calls the clouds to defend the viruses for the homeland.

Yongfeng Yang, Zonggen Peng, and Jiandong Jiang