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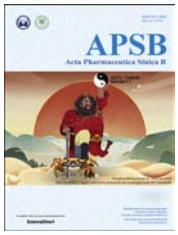

Graphical Abstracts/Acta Pharmaceutica Sinica B, 9 (2019) iii–ix

Reviews

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Repurposing vitamin D for treatment of human malignancies *via* targeting tumor microenvironment

Xu Wu[a], Wei Hu[b], Lan Lu[c], Yueshui Zhao[a], Yejiang Zhou[d], Zhangang Xiao[a], Lin Zhang[a,e], Hanyu Zhang[a], Xiaobing Li[a], Wanping Li[a], Shengpeng Wang[f], Chi Hin Cho[a], Jing Shen[a] Mingxing Li[a]

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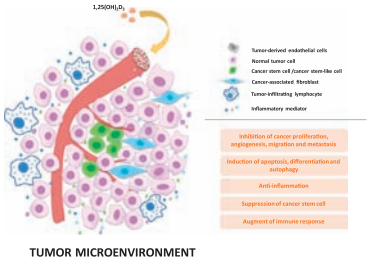

Supplementation of vitamin D is associated with reduced cancer risk and favorable prognosis. Vitamin D not only suppresses cancer cells and cancer stem cells, but also regulates tumor microenvironment, demonstrating the promise of the benefit of vitamin D in cancer prevention and treatment.

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Small molecules for fat combustion: targeting obesity

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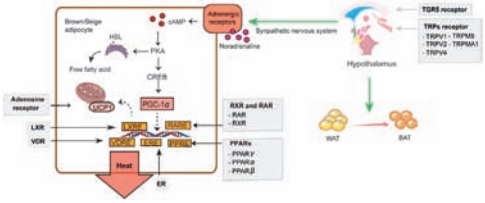

Brown adipose tissue (BAT) and beige cells dissipates fatty acids as heat, termed non-shivering thermogenesis, which has emerged as a potential therapeutically way to treat obesity. The current review provides a comprehensive and up-to-date of knowledge from the biological importance of thermogenesis to the representative thermogenic regulators for treating obesity.

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Marine sponges of the genus *Stelletta* as promising drug sources: chemical and biological aspects

Qihao Wu[a,b], Bastien Nay[c], Min Yang[a], Yeke Ni[a], Hong Wang[b], Ligong Yao[a], Xuwen Li[a]

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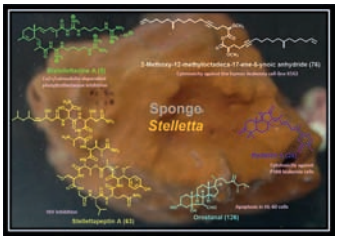

Marine sponges of the genus *Stelletta* are well known as rich sources of diverse and complex natural products with novel structures and broad biological activities, which have attracted a lot of attention from chemists seeking to perform their total synthesis in parallel to intensive biological studies towards new drug leads. In this review, we summarize the chemical and biological aspects of *Stelletta* sponges as promising drug sources.

Original Articles

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The epigallocatechin gallate derivative Y_6 reverses drug resistance mediated by the ABCB1 transporter both *in vitro* and *in vivo*

Yan Wen[a,b,c], Ruiqiang Zhao[a,d], Pranav Gupta[a], Yingfang Fan[a,e], Yunkai Zhang[a], Zhenguang Huang[b], Xiaohui Li[f], Yuangang Su[f], Lijuan Liao[f], Yu-An Xie[g], Donghua Yang[a], Zhe-Sheng Chen[a], Gang Liang[h]

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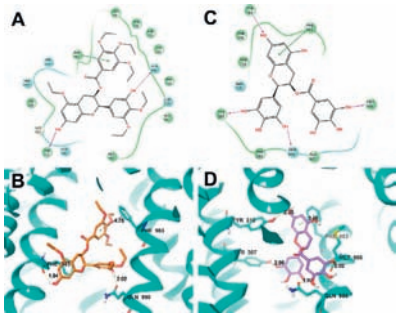

Y_6, an epigallocatechin gallate derivative, reverses ABCB1-mediated multidrug resistance *in vitro* and *in vivo*, and the reversal effect of Y_6 is significantly greater than epigallocatechin gallate.

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LSD1 inhibition suppresses the growth of clear cell renal cell carcinoma *via* upregulating P21 signaling

Liangsong Zhu, Jianfeng Wang, Wen Kong, Jiwei Huang, Baijun Dong, Yiran Huang, Wei Xue, Jin Zhang

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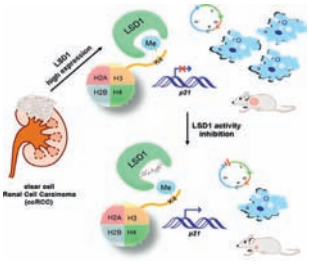

Histone lysine-specific demethylase1 (LSD1) mediates cell proliferation in clear cell renal cell carcinomas (ccRCC). LSD1 is highly expressed in ccRCC samples and it suppresses H3K4 methylation, inducing ccRCC cell proliferation through P21 signaling dysfunction; inhibition of LSD1 restores H3K4 methylation, inducing G1/S cell-cycle arrest by increasing the level of check-point regulator P21.

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Design, synthesis and biological evaluation of chalcone analogues with novel dual antioxidant mechanisms as potential anti-ischemic stroke agents

Jiabing Wang[a,b], Lili Huang[a,c], Chanchan Cheng[a], Ge Li[a], Jingwen Xie[a], Mengya Shen[a], Qian Chen[a], Wulan Li[a,d], Wenfei He[a], Peihong Qiu[a], Jianzhang Wu[a]

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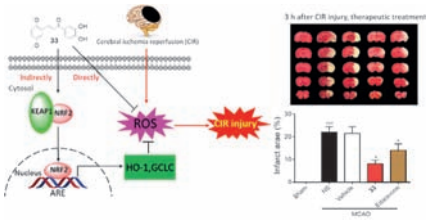

Chalcone analogue **33** conferred protection of PC12 cells against H_2O_2 insult with novel dual-antioxidant mechanism of directly scavenging reactive oxygen species (ROS) and indirectly through antioxidant pathway activation, and the effect of **33** was more pronounced than that of mono-antioxidant mechanism compounds after MCAO and BCAO in animals.

Meeting Report

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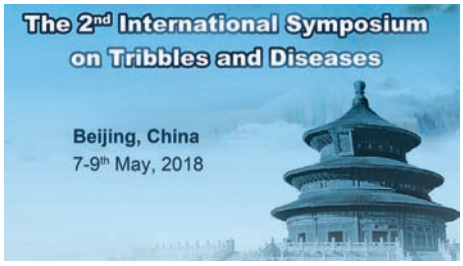
Highlights of the 2nd International Symposium on Tribbles and Diseases: tribbles tremble in therapeutics for immunity, metabolism, fundamental cell biology and cancer

Bing Cui[a], Patrick A. Eyers[b], Leonard L. Dobens[c], Nguan Soon Tan[d,e,f,g], Peter D. Mace[h], Wolfgang A. Link[i,j,k], Endre Kiss-Toth[l], Karen Keeshan[m], Takuro Nakamura[n], Warren S. Pear[o], Yodit Feseha[p,q], Jessica Johnston[l], Arkatiz Carracedo[r,s,t,u], Marcel Scheideler[v,w,x,y], Zabran llyas[l], Robert C. Bauer[z], Jorge D. Erusalimsky[aa], Dominika Grzesik[ab], Juan Salamanca-Viloria[ac,ad], Xiaoxi Lv[a], Yishi Jin[ae], Ke Li[a,af], Guillermo Velasco[ag], Shuang Shang[a], Jose M. Lizcano[ah], Xiaowei Zhang[a], Jichao Zhou[a], Jiaojiao Yu[a], Fang Hua[a], Feng Wang[a], Shanshan Liu[a], Jinmei Yu[a], Zhuowei Hu[a]



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This is a meeting report of the 2nd International Symposium on Tribbles and Diseases held May 7–9, 2018 in Beijing, China. A group of speakers reported their recent findings and disseminated ongoing studies about Tribbles proteins related to immunity, metabolism, fundamental cell biology, cancer, and discussed potential implications for target therapy.

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Cover story

Front

Cancer immunotherapy has recently attracted much attention, which mainly features the administration of antibodies that block the so-called immune checkpoint pathways. Herein, this paper examined the effect of SHP099, an SHP2 allosteric inhibitor, on tumor growth in mouse xenograft models. We found that SHP099 decreased tumor burden *via* triggering $CD8^+$ T cell-mediated anti-tumor immunity. In addition, the combination of SHP099 and anti-PD-1 antibody conferred a higher therapeutic efficacy than either monotherapy alone in controlling tumor growth. The cover paper used Chinese legendary personage Zhong Kui, the ghost buster, for reference. On one hand, anti-tumor immunity is enhanced. On the other hand, tumor growth is inhibited. This study suggests that SHP2 inhibitor SHP099 is a promising drug candidate for cancer immunotherapy.

Xiangbao Meng, Qiang Xu and Yang Sun

Back

Marine sponges are regarded as one of the most important sources of marine natural products (MNPs) with potential therapeutic applications. The sponge of the genus *Stelletta* is widely distributed in the marine ecological system, with alkaloids, triterpenoids, and peptides as its most prominent bioactive secondary metabolites. The widespread biological properties, such as anti-tumor, anti-microbial, and anti-HIV activities, enable *Stelletta*-derived MNPs to possess a broad application space and a bright market foreground in exploiting novel marine drug leads. In this review, we described the discovery of these metabolites and highlighted on the further synthesis and potential applications in future medicinal research of the most promising compounds. The research group of Prof. Yue-wei Guo (GUO LAB) has been engaged in the chemical and biological study of marine invertebrates, including *Stelletta* sponges, from Chinese Sea over 20 years, and this review paper is dedicated to Prof. Yue-wei Guo on the occasion of his 60^{th} birthday, for his pioneer work on Chinese marine natural product chemistry.

Xuwen Li