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Letter to the editor

Inhaled heparin polysaccharide nanodecoy against SARS-CoV-2 and variants
Bin Tu\textsuperscript{a,b}, Huiyuan Wang\textsuperscript{a}, Xinran An\textsuperscript{a,c}, Jingkun Qu\textsuperscript{a,d}, Qianqian Li\textsuperscript{a,e}, Yanrong Gao\textsuperscript{a,b}, Mingjie Shi\textsuperscript{a}, Hong Qiu\textsuperscript{a}, Yongzhuo Huang\textsuperscript{a,b,f,g,h}
\textsuperscript{a}State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China
\textsuperscript{b}University of Chinese Academy of Sciences, Beijing 100049, China
\textsuperscript{c}University of Michigan College of Pharmacy, Ann Arbor, MI 48109, USA
\textsuperscript{d}School of Chinese Materia Medica, Nanjing University of Chinese Medicine, Nanjing 210023, China
\textsuperscript{e}Nanchang University College of Pharmacy, Nanchang 330006, China
\textsuperscript{f}Zhongshan Institute for Drug Discovery, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Zhongshan 528437, China
\textsuperscript{g}NMP A Key Laboratory for Quality Research and Evaluation of Pharmaceutical Excipients, Shanghai 201203, China
\textsuperscript{h}Taizhou University, School of Advanced Study, Institute of Natural Medicine and Health Product, Taizhou 318000, China

The heparin polysaccharide nanoparticles block the interaction between heparan sulfate/S protein and inhibit the infection of both wild-type SARS-CoV-2 pseudovirus and the mutated strains through pulmonary delivery.

Commentary

Viral miRNA-mediated activation of hyaluronan production as a drug target against COVID-19
Shuai Yang\textsuperscript{a,b}, Lu Chen\textsuperscript{a,b}, Ying Tong\textsuperscript{a,b}, Wenqiang Yu\textsuperscript{a,b}
\textsuperscript{a}Laboratory of RNA Epigenetics, Institutes of Biomedical Sciences & Shanghai Public Health Clinical Center & Department of General Surgery, Huashan Hospital, Cancer Metastasis Institute, Shanghai Medical College, Fudan University, Shanghai 200040, China
\textsuperscript{b}Shanghai Key Laboratory of Medical Epigenetics, Shanghai 200032, China

Correction

Author correction to ‘Ruscogenin alleviates LPS-triggered pulmonary endothelial barrier dysfunction through targeting NMMHC IIA to modulate TLR4 signaling’ [Acta Pharmaceutica Sinica B 12 (2022) 1198–1212]
Yunhao Wu, Xiu Yu, Yuwei Wang, Yalin Huang, Jiahui Tang, Shuaishuai Gong, Siyu Jiang, Yuanli Xia, Fang Li, Boyang Yu, Yuanyuan Zhang, Junping Kou
State Key Laboratory of Natural Medicines, Jiangsu Key Laboratory of TCM Evaluation and Translational Research, Department of Pharmacology of Chinese Materia Medica, School of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing 211198, China

Cover story

Front

Development of one successful drug takes 10–15 years and costs $1–2 billion. Despite implementation of many successful strategies, 90% clinical drug development fails. The perspective by Sun et al. reviewed the successful strategies and identified the overlooked gaps in the current drug development process. Based on the analysis, they proposed a structure–tissue exposure/selectivity/activity relationship (STAR) system to improve drug optimization, drug candidate selection, and dose optimization in clinical studies. STAR system classifies drug candidates to four different classes (classes I–IV) based on drug’s potency/selectivity (SAR), tissue exposure/selectivity (STR), and required dose for balancing clinical efficacy/toxicity. The four different classes of drug candidates require different strategies to select lead drug candidates, optimize clinical doses, and balance clinical efficacy/toxicity. Successful application of STAR will improve the efficiency of drug optimization and clinical studies for four different classes of drug candidates to improve the success rate of clinical drug development.

Duxin Sun, et al.

Back

PDE8 belongs to a superfamily of PDE in charge of hydrolyzing the second messengers, and shows the strongest affinity for cAMP. Inhibition of PDE8 may be a novel therapeutic strategy for cognitive disorders like vascular dementia (VaD). However, only a few PDE8 inhibitors have been developed yet. Herein, structure-based discovery resulted in a non-chiral, orally active (\textit{F} = 100\%), and selective PDE8 inhibitor $15$ with an IC$_{50}$ of 11 nmol/L. Its coecystal with PDE8 revealed that $15$ might involve distinctive interactions with H-pocket including T-shaped $\pi$–$\pi$ interaction with Phe785 and a unique H-bond network, which have never been observed in a PDE-inhibitor complex before. Oral administration of $15$ significantly improved the cAMP level of the right brain in VaD mice, and thus exhibited notable and dose-dependent therapeutic effects on cognitive improvement, which validated PDE8 as a potential target for VaD.

Yimao Wu, Hai-Bin Luo, et al.