

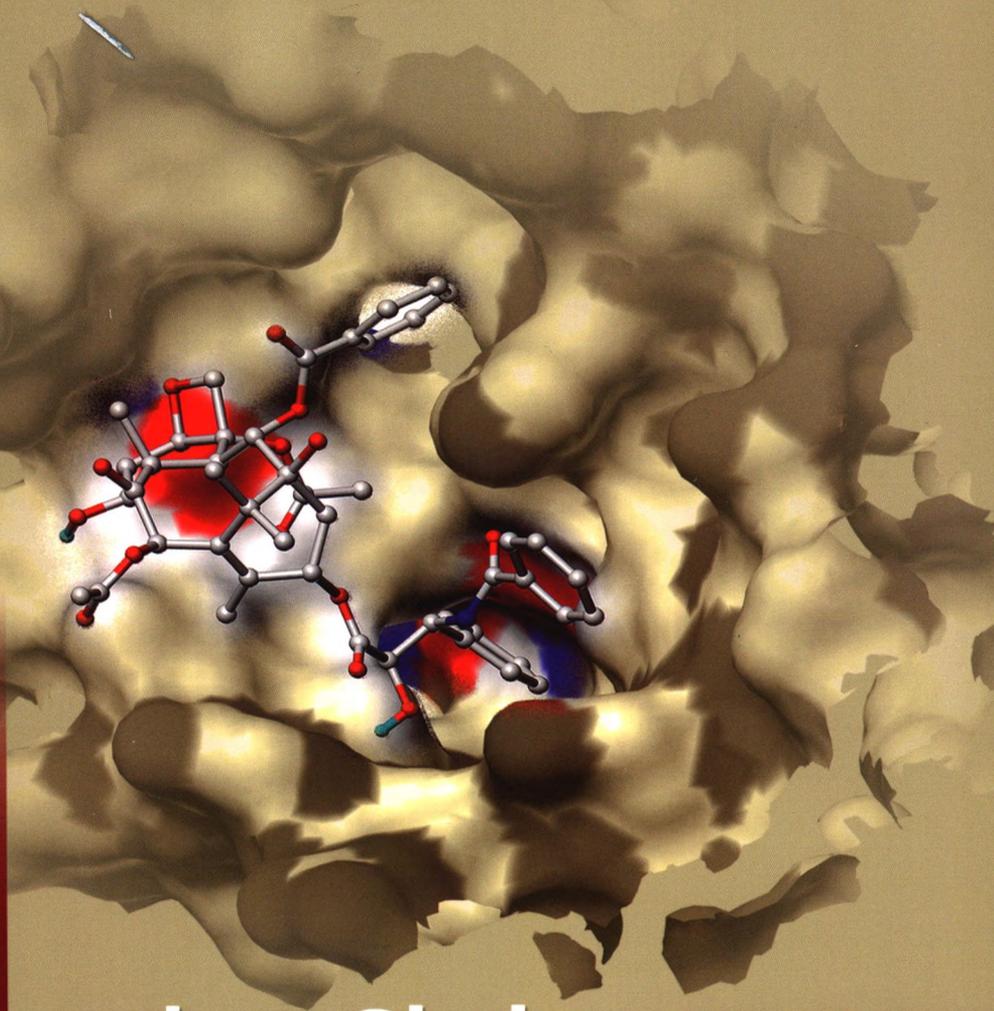


# 药 学 学 报

第55卷

第4期

2020 Vol. 55 No. 4



# Acta Pharmaceutica Sinica

抗病毒药物化学研究进展专刊

展 鹏, 刘新泳等

冠状病毒抑制剂研究的药物化学策略  
万方数据

刘新泳, 展 鹏等

天然产物抗病毒药物的研究进展



中国药学会  
中国医学科学院药物研究所

# 药 学 学 报

第 55 卷 第 4 期 2020 年 4 月

## 抗病毒药物化学研究进展专刊 图 文 摘 要

### 综 述

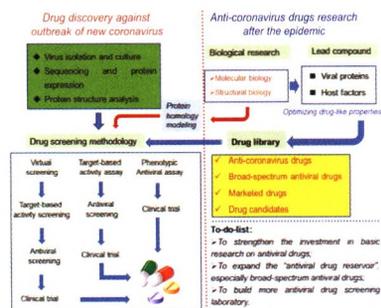
537

#### 冠状病毒抑制剂研究的药物化学策略

李敬<sup>1,2</sup>, 姜向毅<sup>1,2</sup>, 徐淑静<sup>1,2</sup>, 崔清华<sup>3</sup>, 杜瑞坤<sup>3</sup>, 康东伟<sup>1,2</sup>, 展鹏<sup>1,2\*</sup>, 荣立军<sup>4\*</sup>, 刘新泳<sup>1,2\*</sup>

(1. 山东大学药学院药物化学研究所, 山东 济南 250012; 2. 山东省中比抗病毒创新药物合作研究中心, 山东 济南 250012; 3. 山东中医药大学药学院, 山东 济南 250355; 4. 美国伊利诺伊大学芝加哥校区医学院微生物学与免疫学系, 伊利诺伊州芝加哥 60612)

本文从药物化学的视角, 精选抗冠状病毒药物的研究案例, 总结了药物发现策略, 提出了未来研究的新思路。



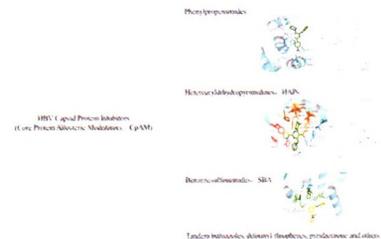
554

#### 基于新靶标的 HBV 抑制剂研究进展 (1): 衣壳蛋白抑制剂

马悦<sup>1</sup>, 魏粉菊<sup>1</sup>, 俞霁<sup>1</sup>, 贾海永<sup>2</sup>, 刘新泳<sup>1\*</sup>, 展鹏<sup>1\*</sup>

(1. 山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012; 2. 潍坊医学院药学院, 山东 潍坊 261053)

本文从药物化学的视角综述了不同结构类型的 HBV 衣壳蛋白抑制剂的研究进展。



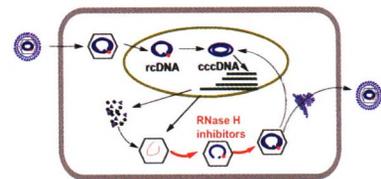
566

#### 基于新靶标的 HBV 抑制剂研究进展 (2): RNase H 及其他靶标

魏粉菊<sup>1</sup>, 马悦<sup>1</sup>, 俞霁<sup>1</sup>, 贾海永<sup>2</sup>, 刘新泳<sup>1\*</sup>, 展鹏<sup>1\*</sup>

(1. 山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012; 2. 潍坊医学院药学院, 山东 潍坊 261053)

本综述从药物化学的视角总结了基于 RNase H 等新靶标的抗 HBV 抑制剂研究进展。



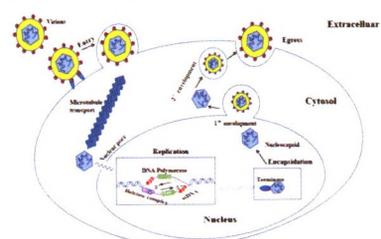
575

#### 抗疱疹病毒药物化学研究新进展

魏文秀, 荆兰兰, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文系统综述了抗疱疹病毒药物的研究历史与现状。



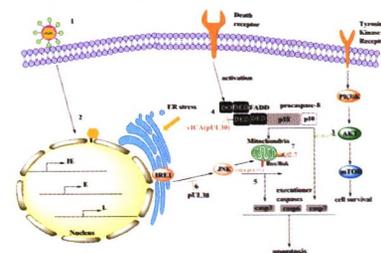
585

#### 人巨细胞病毒抑制剂研究进展

李敬, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文从药物化学角度总结了抗 HCMV 药物的新靶标及其研究进展。



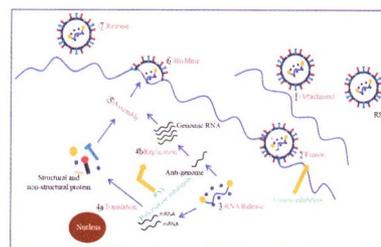
597

呼吸道合胞病毒抑制剂研究新进展

徐淑静, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文精选典型研究案例, 从药物化学的角度综述了不同靶点 RSV 抑制剂的研究进展。



The replication cycle of RSV and drug targets

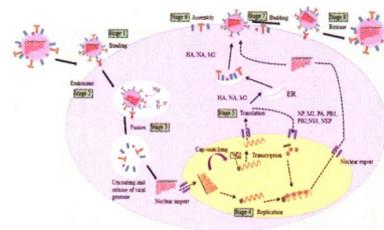
611

抗流感病毒药物靶标及其小分子抑制剂的研究进展

修思雨<sup>1</sup>, 张健<sup>1</sup>, 鞠翰<sup>1</sup>, 贾瑞芳<sup>1</sup>, 黄兵<sup>2</sup>, 展鹏<sup>1\*</sup>, 刘新泳<sup>1\*</sup>

(1. 山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012; 2. 山东省农业科学院家禽研究所, 山东 济南 250012)

本综述精选近几年最具代表性的研究实例, 从药物化学的视角总结了抗流感病毒新靶标及其小分子抑制剂的研究进展。



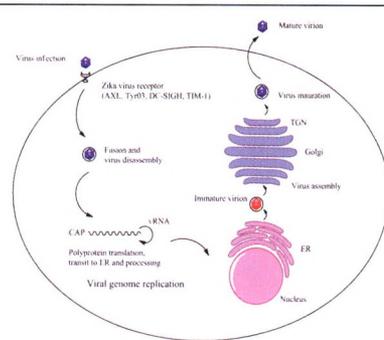
627

寨卡病毒抑制剂研究新进展

李卓, 贾瑞芳, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本综述总结了近几年抗寨卡病毒感染药物研究的新进展, 并对该领域的研究趋势进行了展望。



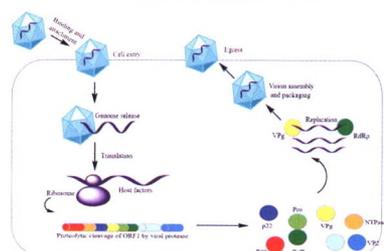
640

抗诺如病毒药物及其疫苗研究新进展

董悦, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本综述通过精选代表性研究实例, 总结了抗 NoV 药物及其疫苗的最新进展。



The replication cycle of NoV

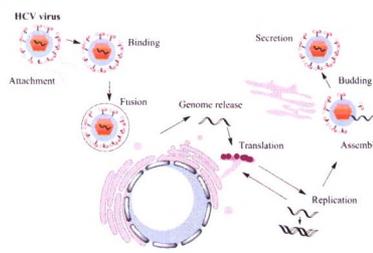
652

丙型肝炎病毒抑制剂研究进展

宋淑, 高萍, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本综述精选近几年具代表性的研究实例, 从药物化学的视角总结了抗丙肝小分子抑制剂的前沿进展。



The replication cycle of HCV

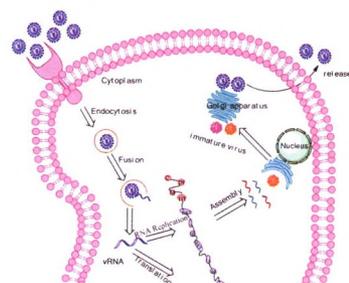
669

抗登革病毒药物化学研究新进展

侯凌欣, 鞠翰, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文概述了抗登革病毒的结构, 致病机制以及针对不同靶点的抗登革药物的研究新进展。



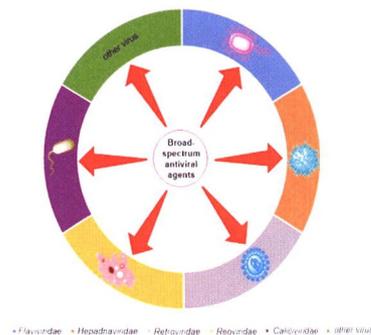
679

广谱抗病毒药物研究进展

黄天广, 孙林, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文总结了广谱抗病毒药物的最新进展, 为今后病毒感染性疾病的药物研发提供参考。



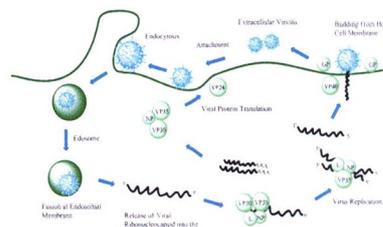
694

埃博拉病毒抑制剂研究新进展

任玉洁, 张硕, 魏粉菊, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文根据病毒感染复制周期介绍了埃博拉病毒 (EBOV) 药物靶点及其小分子抑制剂。



703

天然产物抗病毒药物的研究进展

付志鹏, 周忠霞, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文综述总结了近十年来具有抗病毒活性的天然产物, 为药物开发提供有潜力的先导化合物。



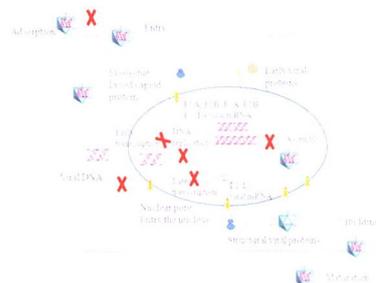
720

抗腺病毒药物化学研究新进展

孙彦莹, 左晓芳, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文从药物化学的角度总结了抗腺病毒药物新靶标及其抑制剂的前沿进展。



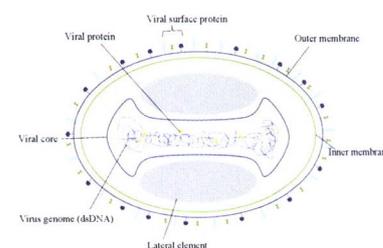
734

抗痘病毒药物化学研究新进展

张涛, 周忠霞, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文从药物化学的角度总结了抗痘病毒药物新靶标及其抑制剂的前沿进展。



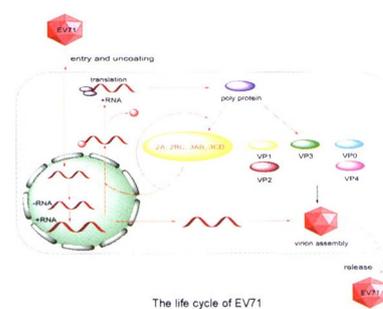
744

抗肠病毒 71 型药物化学新进展

陶昱岑, 郝霞, 刘新泳\*, 展鹏\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文从药物化学视角总结了近年来抗肠病毒 71 型药物的研究进展。



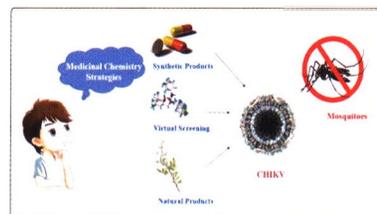
754

**基孔肯雅病毒抑制剂研究进展**

姜向毅, 李敬, 魏晓颖, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文综述了基孔肯雅病毒抑制剂研究的新进展, 并概述了发现这些小分子化合物的药物化学策略。



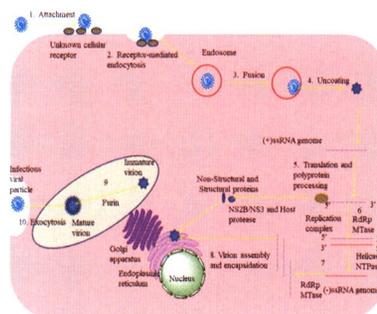
763

**西尼罗病毒抑制剂研究进展**

梁瑞鹏, 赵彤, 展鹏\*, 刘新泳\*

(山东大学药学院药物化学研究所, 化学生物学教育部重点实验室, 山东 济南 250012)

本文根据西尼罗病毒的主要靶点, 总结了西尼罗病毒抑制剂研究的新进展。



# ACTA PHARMACEUTICA SINICA

Volume 55 Number 4 2020 April

## Progress in Chemical Research of Antiviral Drugs Graphical Abstracts

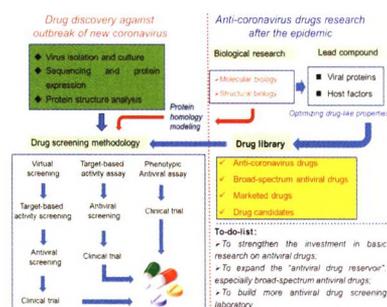
### Reviews

537

#### Medicinal chemistry strategies in seeking coronavirus inhibitors

LI Jing<sup>1,2</sup>, JIANG Xiang-yi<sup>1,2</sup>, XU Shu-jing<sup>1,2</sup>, CUI Qing-hua<sup>3</sup>, DU Rui-kun<sup>3</sup>,  
KANG Dong-wei<sup>1,2</sup>, ZHAN Peng<sup>1,2\*</sup>, RONG Li-jun<sup>4\*</sup>, LIU Xin-yong<sup>1,2\*</sup>

(1. Department of Medicinal Chemistry, School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China; 2. China-Belgium Collaborative Research Center for Innovative Antiviral Drugs of Shandong Province, Jinan 250012, China; 3. College of Pharmacy, Shandong University of Traditional Chinese Medicine, Jinan 250355, China; 4. Department of Microbiology and Immunology, College of Medicine, University of Illinois at Chicago, Chicago, IL 60612, USA)



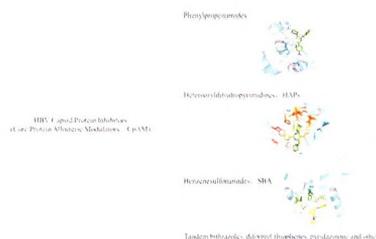
This article reviews the drug discovery strategies of anti-coronavirus drugs from the perspective of medicinal chemistry, and tries to provide some clues to future research.

554

#### Advances in research on HBV inhibitors based on new targets (1): capsid protein inhibitors

MA Yue<sup>1</sup>, WEI Fen-ju<sup>1</sup>, YU Ji<sup>1</sup>, JIA Hai-yong<sup>2</sup>, LIU Xin-yong<sup>1\*</sup>, ZHAN Peng<sup>1\*</sup>

(1. Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China; 2. School of Pharmacy, Weifang Medical University, Weifang 261053, China)



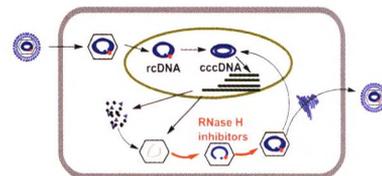
This paper reviews the research progress of HBV capsid protein inhibitors with different structural types from the perspective of medicinal chemistry.

566

#### Advances in research on HBV inhibitors based on new targets (2): RNase H and others

WEI Fen-ju<sup>1</sup>, MA Yue<sup>1</sup>, YU Ji<sup>1</sup>, JIA Hai-yong<sup>2</sup>, LIU Xin-yong<sup>1\*</sup>, ZHAN Peng<sup>1\*</sup>

(1. Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China; 2. School of Pharmacy, Weifang Medical University, Weifang 261053, China)



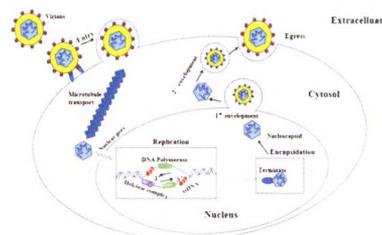
We summarize and discuss current endeavours towards the discovery and development of anti-HBV agents towards novel drug targets, exemplified by RNase H.

575

#### New progress in medicinal chemistry of anti-herpesviruses drug research

WEI Wen-xiu, JING Lan-lan, LIU Xin-yong<sup>\*</sup>, ZHAN Peng<sup>\*</sup>

(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)



This paper systematically reviews the research history and current situation of anti-herpesvirus drugs.

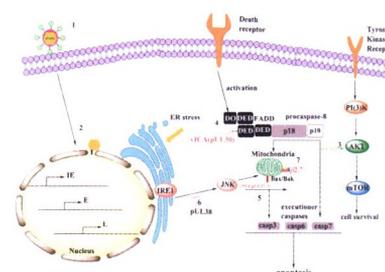
585

**Advances in human cytomegalovirus inhibitors**

LI Jing, LIU Xin-yong\*, ZHAN Peng\*

(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)

This paper summarizes the new targets and research progress of anti-HCMV infection from the prospect of medicinal chemistry.



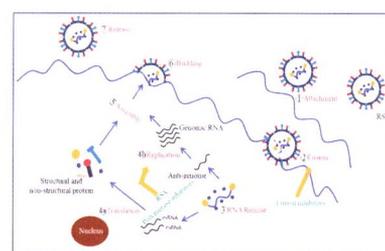
597

**New progress in research on respiratory syncytial virus inhibitors**

XU Shu-jing, LIU Xin-yong\*, ZHAN Peng\*

(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)

This paper selects typical case studies and reviews the research progress of anti-respiratory syncytial virus inhibitors from the perspective of medicinal chemistry.



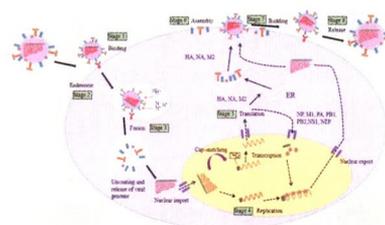
The replication cycle of RSV and drug targets

611

**Progress on IFV drug targets and small molecule inhibitors**XIU Si-yu<sup>1</sup>, ZHANG Jian<sup>1</sup>, JU Han<sup>1</sup>, JIA Rui-fang<sup>1</sup>, HUANG Bing<sup>2</sup>, ZHAN Peng<sup>1\*</sup>, LIU Xin-yong<sup>1\*</sup>

(1. Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China; 2. Institute of Poultry Science, Shandong Academy of Agricultural Sciences, Jinan 250012, China)

From the point of view of medicinal chemistry, this review summarizes and discusses current endeavours towards the discovery and development of novel influenza inhibitors and also provides examples illustrating new methodologies that contribute to the identification of novel anti-influenza drugs.



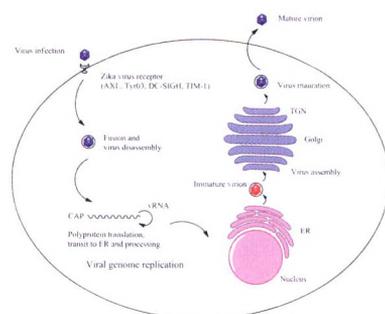
627

**Progress on the discovery and development of anti-zika virus agents**

LI Zhuo, JIA Rui-fang, ZHAN Peng\*, LIU Xin-yong\*

(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)

This review summarizes progress on anti-zika virus drug research and provides prospects in this field.



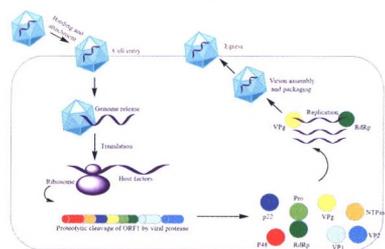
640

**New progress in anti-norovirus drugs and vaccines**

DONG Yue, ZHAN Peng\*, LIU Xin-yong\*

(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)

This review selects the most representative research examples and provides an overview of recent advances in anti-norovirus drugs and vaccines.



The replication cycle of NoV

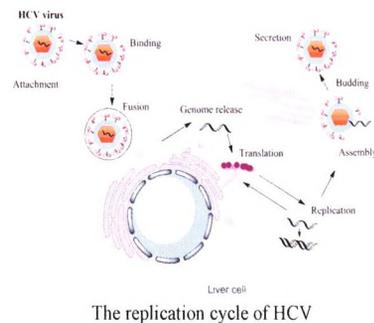
652

**Recent progress in inhibitors against hepatitis C virus**

SONG Shu, GAO Ping, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

From the point of view of medicinal chemistry, we summarize and discuss current endeavors towards the discovery and development of novel HCV inhibitors with various scaffolds or distinct mechanisms of action.



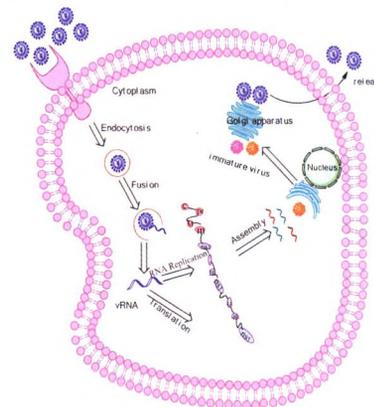
669

**Recent advances in the discovery of dengue virus inhibitors**

HOU Ling-xin, JU Han, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This paper summarizes the structure and pathogenic mechanism of anti-dengue virus and the new research progress of anti-dengue drugs targeting different targets.



679

**Recent advances in the research of broad-spectrum antiviral agents**

HUANG Tian-guang, SUN Lin, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This review summarizes recent advances in the research of broad-spectrum antiviral drugs for the purpose of providing references for development of antiviral drugs in the future.



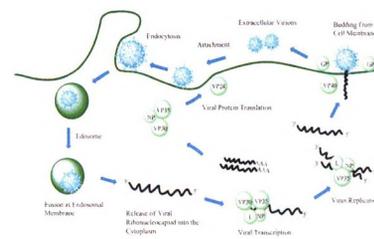
694

**Recent advances in the discovery and development of Ebola virus inhibitors**

REN Yu-jie, ZHANG Shuo, WEI Fen-ju, LIU Xin-yong\*, ZHAN Peng\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This article describes recent advances in the discovery and development of Ebola virus inhibitors based on drug targets in the viral replication cycle.



703

**Advances in the study of antiviral natural products**

FU Zhi-peng, ZHOU Zhong-xia, LIU Xin-yong\*, ZHAN Peng\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This article reviews the progress of antiviral natural products discovered in the past decade to provide potential lead compounds for drug development.



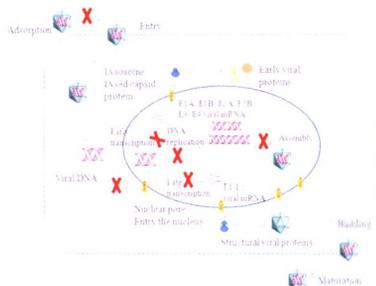
720

**Recent advances in the discovery and development of adenovirus inhibitors**

SUN Yan-ying, ZUO Xiao-fang, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This review summarizes the latest advances in new targets and inhibitors of anti-adenoviral drugs from the perspective of medicinal chemistry.



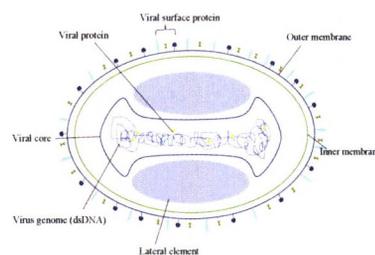
734

**New progress in medicinal chemistry of anti-poxvirus drugs research**

ZHANG Tao, ZHOU Zhong-xia, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This review summarizes the latest advances in new targets and inhibitors of anti-poxvirus drugs from the perspective of medicinal chemistry.



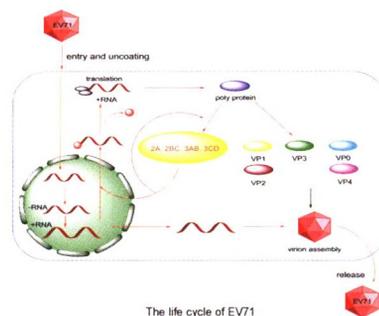
744

**New advances in the discovery of anti-enterovirus-71 agents**

TAO Yu-cen, HAO Xia, LIU Xin-yong\*, ZHAN Peng\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

This paper summarizes the research progress of anti-enterovirus-71 drugs in recent years from the perspective of medicinal chemistry.



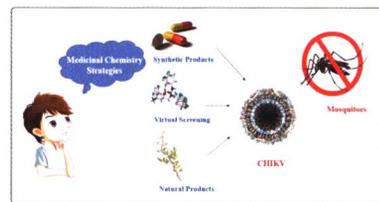
754

**Advances in Chikungunya virus inhibitors**

JIANG Xiang-yi, LI Jing, WEI Xiao-ying, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

We reviewed the recent progress in the study of Chikungunya virus inhibitors, and summarized the medicinal chemistry strategies for discovering small molecule compounds.



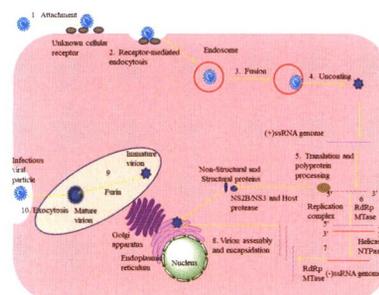
763

**Research progress on the West Nile virus inhibitors**

LIANG Rui-peng, ZHAO Tong, ZHAN Peng\*, LIU Xin-yong\*

*(Department of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, Jinan 250012, China)*

In this article, based on the main targets of West Nile virus, we summarize the new progress research on West Nile virus inhibitors.



# ACTA PHARMACEUTICA SINICA

Volume 55 Number 4 2020 April



期刊基本参数: CN 11-2163/R\*1953\*m\*A4\*236\*zh\*P\* ¥40.00\* \*19\*2020-04

本期责任编辑 郭焕芳

药学学报 (YAOXUE XUEBAO)

(月刊, 1953年7月创刊)

主管单位: 中国科学技术协会

主办单位: 中国药学会 (<http://www.cpa.org.cn>)

中国医学科学院药物研究所

(<http://www.imm.ac.cn>)

编辑出版: 药学报编辑部 (100050 北京市先农坛街1号)

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主编: 王晓良

印刷: 北京科信印刷有限公司

国内订购: 全国各地邮电局

发行范围: 公开发行

国内: 北京报刊发行局

国外: 中国国际图书贸易集团有限公司

(北京市399信箱, 100044)

ACTA PHARMACEUTICA SINICA

(Monthly, Founded in 1953 July)

Directed by: China Association for Science and Technology

Sponsored by: Chinese Pharmaceutical Association

(<http://www.cpa.org.cn>)

Institute of Materia Medica, Chinese Academy of Medical Sciences (<http://www.imm.ac.cn>)

Edited and Published by: Editorial Office of Acta Pharmaceutica Sinica

(1 Xiannongtan Street, Beijing 100050).

Tel / Fax: 86-10-63026192, 63035012;

E-mail: [yxxb@imm.ac.cn](mailto:yxxb@imm.ac.cn); <http://www.yxxb.com.cn>

Editor-in-chief: WANG Xiao-liang

Printed by: Beijing Kexin Printing Co., Ltd.

Domestic subscriptions: Local Post Offices

Distribution

Domestic: Beijing Post Offices

Foreign: China International Book Trading Corporation,

PO Box 399, Beijing 100044, China

ISSN 0513-4870

CN 11-2163/R

2020年 第55卷 第4期

2020, Vol. 55, No.4

2020年4月12日出版

Publication Date: 2020-04-12

邮发代号: 2-233

Code number: M105

国内定价: 每期40.00元



万方数据

ISSN 0513-4870



9 770513 487209