

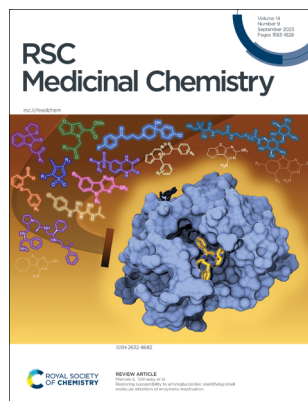
RSC Medicinal Chemistry

rsc.li/medchem

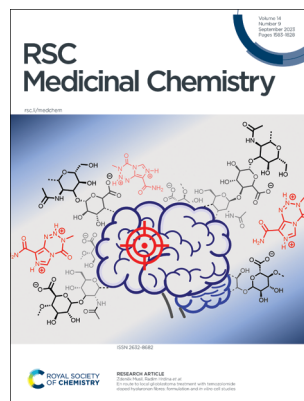
The Royal Society of Chemistry is the world's leading chemistry community. Through our high impact journals and publications we connect the world with the chemical sciences and invest the profits back into the chemistry community.

IN THIS ISSUE

ISSN 2632-8682 CODEN RMCSCX 14(9) 1583-1828 (2023)



Cover
See Marcelo E. Tolmasky *et al.*, pp. 1591–1602.
Image reproduced by permission of Marcelo E. Tolmasky and Prem Chapagain from *RSC Med. Chem.*, 2023, **14**, 1591.



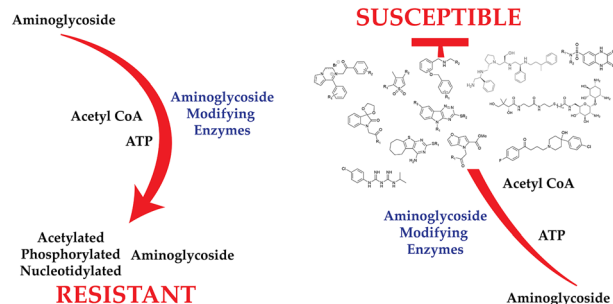
Inside cover
See Zdeněk Musil, Radim Hrdina *et al.*, pp. 1662–1666.
Image designed by Matthew Todd and reproduced by permission of Radim Hrdina from *RSC Med. Chem.*, 2023, **14**, 1662.

REVIEWS

1591

Restoring susceptibility to aminoglycosides: identifying small molecule inhibitors of enzymatic inactivation

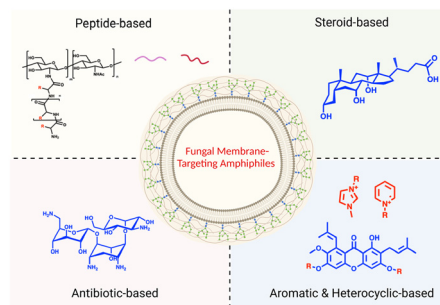
Angel J. Magaña, Jan Sklenicka, Clemencia Pinilla, Marc Giulianotti, Prem Chapagain, Radleigh Santos, Maria Soledad Ramirez and Marcelo E. Tolmasky*



1603

Recent developments in membrane targeting antifungal agents to mitigate antifungal resistance

Devashish Mehta, Varsha Saini and Avinash Bajaj*



Editorial Staff**Executive Editor**

Katie Lim

Deputy Editor

Jack Washington

Editorial Production Manager

Sarah Whitehouse

Development Editor

Emily Cuffin-Munday

Publishing Editors

Nicola Burton, Tom Cozens, Katie Fernandez, Ryan Kean, Roxane Owen

Editorial Assistant

Amy Cook

Publishing Assistant

Andrea Whiteside

Publisher

Sam Keltie

For queries about submitted papers, please contact Sarah Whitehouse, Editorial Production Manager, in the first instance. E-mail medchem@rsc.org

For pre-submission queries please contact Katie Lim, Executive Editor. E-mail medchem-rsc@rsc.org

RSC Medicinal Chemistry (electronic: ISSN 2632-8682) is published 12 times a year by the Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge, UK CB4 0WF.

All orders, with cheques made payable to the Royal Society of Chemistry, should be sent to the Royal Society of Chemistry Order Department, Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge, CB4 0WF, UK

Tel +44 (0)1223 432398; E-mail orders@rsc.org

2023 Annual (electronic) subscription price: £1643; US\$2435. Customers in Canada will be subject to a surcharge to cover GST. Customers in the EU subscribing to the electronic version only will be charged VAT.

If you take an institutional subscription to any Royal Society of Chemistry journal you are entitled to free, site-wide web access to that journal. You can arrange access via Internet Protocol (IP) address at www.rsc.org/ip

Customers should make payments by cheque in sterling payable on a UK clearing bank or in US dollars payable on a US clearing bank.

Whilst this material has been produced with all due care, the Royal Society of Chemistry cannot be held responsible or liable for its accuracy and completeness, nor for any consequences arising from any errors or the use of the information contained in this publication. The publication of advertisements does not constitute any endorsement by the Royal Society of Chemistry or Authors of any products advertised. The views and opinions advanced by contributors do not necessarily reflect those of the Royal Society of Chemistry which shall not be liable for any resulting loss or damage arising as a result of reliance upon this material. The Royal Society of Chemistry is a charity, registered in England and Wales, Number 207890, and a company incorporated in England by Royal Charter (Registered No. RC000524), registered office: Burlington House, Piccadilly, London W1J 0BA, UK, Telephone: +44 (0) 207 4378 6556.

Advertisement sales:

Tel +44 (0) 1223 432246; Fax +44 (0) 1223 426017;

E-mail advertising@rsc.org

For marketing opportunities relating to this journal, contact marketing@rsc.org

RSC Medicinal Chemistry

rsc.li/medchem

RSC Medicinal Chemistry publishes significant research and review articles in medicinal chemistry and related drug discovery science.

Editorial Board**Editor-in-Chief**

Mike Waring, Newcastle University, UK

Associate Editors

Cynthia Dowd, George Washington University, USA

Maria Duca, Université Côte d'Azur - CNRS, France

Sally-Ann Poulsen, Griffith University, Queensland, Australia

Jian Zhang, Shanghai Jiao Tong University School of Medicine, China

Members

Hayley Binch, Hoffmann-La Roche, Switzerland

Paola Castaldi, LifeMine Therapeutics, USA
Matthew Fuchter, Imperial College London, UK

Lyn Jones, Dana-Farber Cancer Institute, Boston, USA

Jean-Louis Reymond, University of Bern, Switzerland

Advisory Board

Timor Baasov, Israel Institute of Technology, Israel

Andreas Bender, University of Cambridge, UK
Julian Blagg, Institute of Cancer Research, Sutton, UK

Margaret Brimble, University of Auckland, New Zealand

Mark Bunnage, Vertex Pharmaceuticals, USA
Christopher Burns, Certa Therapeutics, Australia

Andrea Cavalli, University of Bologna, Italy
Young-Tae Chang, POSTECH, South Korea

James Crawford, Genentech, Inc., USA
Matthew Duncton, Rigel Pharmaceuticals Inc, San Francisco, USA

Stephen Frye, University of North Carolina at Chapel Hill, USA

Sylvie Garneau-Tsodikova, University of Kentucky, USA

Barry Gold, University of Pittsburgh, USA
Jayanta Haldar, Jawaharlal Nehru Centre for Advanced Scientific Research, India

Gyoonhee Han, Yonsei University, Korea
Mike Hann, GSK Medicine Research Centre, UK

Christian Heinis, EPFL, Switzerland
Laura H. Heitman, Leiden University, Netherlands

Yoshinori Ikeura, Axcel Drug Discovery Partners, Japan

Ahmed Kamal, NIPER, Hyderabad, India
Bob (Robert) Langer, MIT, USA

Steven V. Ley, University of Cambridge, UK

María Luz López Rodríguez, Complutense University of Madrid, Spain

Christa Müller, University of Bonn, Germany
Roberto Pellicciari, University of Perugia, Italy
David Rees, Astex Therapeutics, Cambridge, UK

Motonari Uesugi, Kyoto University, Japan
John C. Vederas, University of Alberta, Canada

Paul Wender, Stanford University, USA
Zhen Yang, Peking University, China
Ming-Qiang Zhang, Amgen, Shanghai, China

Information for Authors

Full details on how to submit material for publication in RSC Medicinal Chemistry are given in the Instructions for Authors (available from <http://www.rsc.org/authors>). Submissions should be made via the journal's homepage: rsc.li/medchem

Authors may reproduce/republish portions of their published contribution without seeking permission from the Royal Society of Chemistry, provided that any such republication is accompanied by an acknowledgement in the form: (Original Citation)–Reproduced by permission of the Royal Society of Chemistry.

This journal is © The Royal Society of Chemistry 2023.

Apart from fair dealing for the purposes of research or private study for non-commercial purposes, or criticism or review, as permitted under the Copyright, Designs and Patents Act 1988 and the Copyright and Related Rights Regulation 2003, this publication may only be reproduced, stored or transmitted, in any form or by any means, with the prior permission in writing of the Publishers or in the case of reprographic reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency in the UK. US copyright law is applicable to users in the USA.

Registered Charity No. 207890.

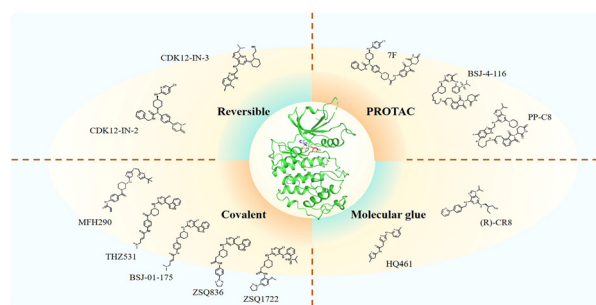


REVIEWS

1629

Research progress of anticancer drugs targeting CDK12

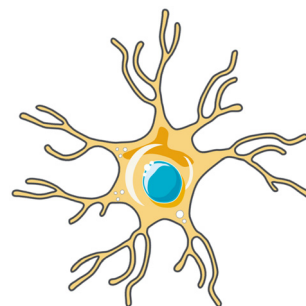
Zhijia Yan, Yongli Du,* Haibin Zhang, Yong Zheng, Huiting Lv, Ning Dong and Fang He



1645

Druggable targets for the immunopathy of Alzheimer's disease

Donald F. Weaver*

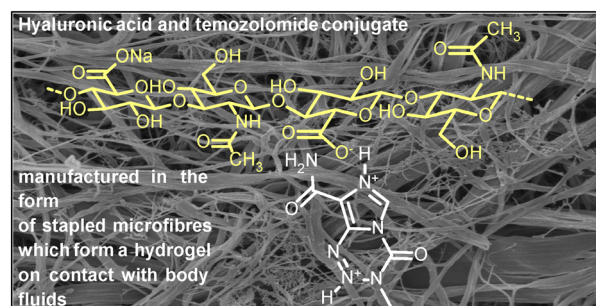


RESEARCH ARTICLES

1662

En route to local glioblastoma treatment with temozolomide doped hyaluronan fibres: formulation and *in vitro* cell studies

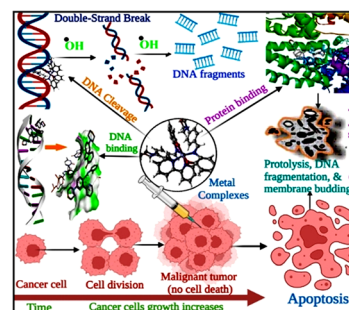
Marie Belhajová, Aleš Vicha, Ladislav Burgert, Iveta Brožková, Ludmila Michalíčková, Radim Hrdina, Tomáš Moravec, David Netuka, Zdeněk Musil* and Radim Hrdina*



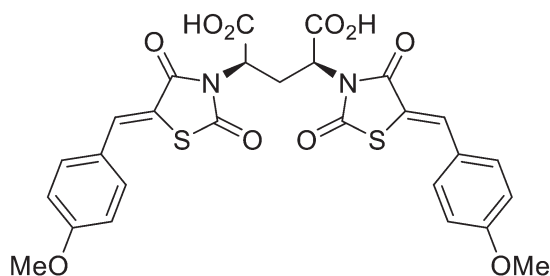
1667

Exploring the antioxidant, antimicrobial, cytotoxic and biothermodynamic properties of novel morpholine derivative bioactive Mn(II), Co(II) and Ni(II) complexes – combined experimental and theoretical measurements towards DNA/BSA/SARS-CoV-2 3CL^{Pro}

Karunganathan Sakthikumar, Bienfait Kabuyaya Isamura and Rui Werner Maçedo Krause*



1698

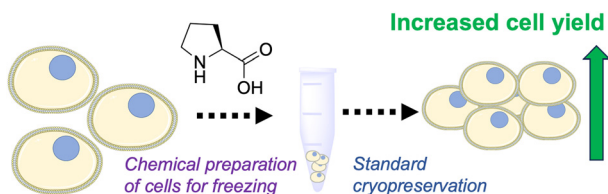


Compound 5b

Enhancing allosteric inhibition of dihydrodipicolinate synthase through the design and synthesis of novel dimeric compounds

Rebecca M. Christoff, Mohammad Al Bayer, Tatiana P. Soares da Costa, Matthew A. Perugini and Belinda M. Abbott*

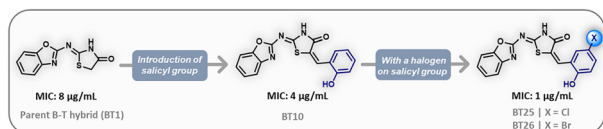
1704



Proline pre-conditioning of Jurkat cells improves recovery after cryopreservation

Alex Murray, Peter Kilbride and Matthew I. Gibson*

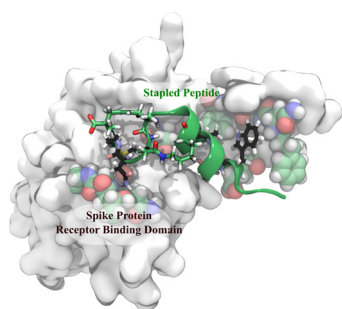
1712



Discovery of benzoxazole-thiazolidinone hybrids as promising antibacterial agents against *Staphylococcus aureus* and *Enterococcus* species

Vijay Sai Krishna Cheerla, Abdul Akhir, Deepanshi Saxena, Rahul Maitra, Sidharth Chopra* and Sundaresan Chittor Neelakantan*

1722



De novo design of a stapled peptide targeting SARS-CoV-2 spike protein receptor-binding domain

Ravindra Thakkar,* Dilip K. Agarwal, Chathuranga B. Ranaweera, Susumu Ishiguro, Martin Conda-Sheridan, Natasha N. Gaudreault, Juergen A. Richt, Masaaki Tamura and Jeffrey Comer

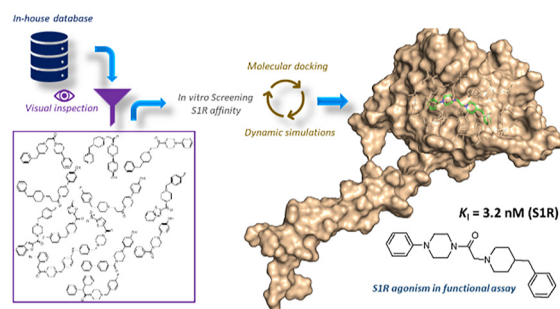


RESEARCH ARTICLES

1734

Discovery and computational studies of piperidine/piperazine-based compounds endowed with sigma receptor affinity

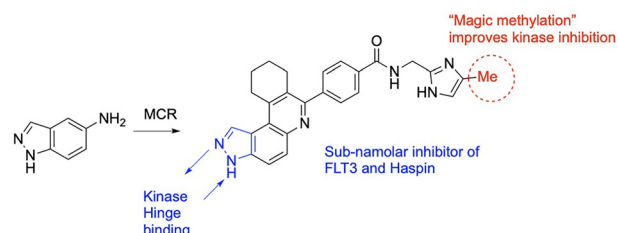
Laura De Luca, Lisa Lombardo, Salvatore Mirabile, Agostino Marrazzo, Maria Dichiara, Giuseppe Cosentino, Emanuele Amata and Rosaria Gitto*



1743

Dual FLT3/haspin kinase inhibitor based on 3H-pyrazolo[4,3-f]quinoline scaffold with activities against acute myeloid leukemia

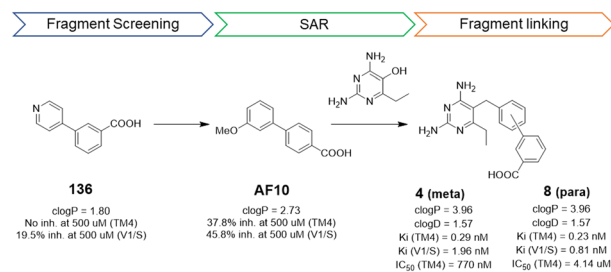
Allison L. Kempen, Nickolas R. Brauer and Herman O. Sintim*



1755

Discovery of rigid biphenyl *Plasmodium falciparum* DHFR inhibitors using a fragment linking strategy

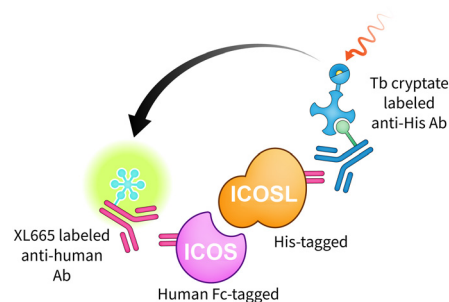
Marie Hoarau,* Patpanat Sermmmai, Thaveechai Varatthan, Ratthiya Thiabma, Tararat Jantra, Roonglawan Rattanajak, Danoo Vitsupakorn, Jarunee Vanichtanankul, Siriporn Saepua, Yongyuth Yuthavong, Chawanee Thongpanchang and Sumalee Kamchonwongpaisan



1767

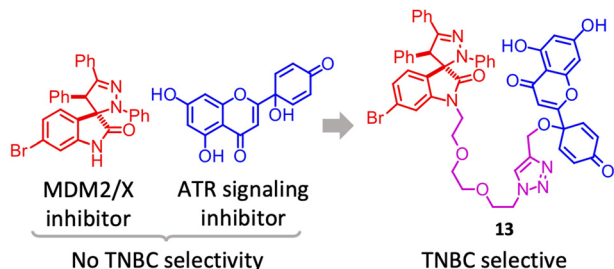
First-in-class small molecule inhibitors of ICOS/ICOSL interaction as a novel class of immunomodulators

Somaya A. Abdel-Rahman, Katarzyna Świderek and Moustafa T. Gabr*



RESEARCH ARTICLES

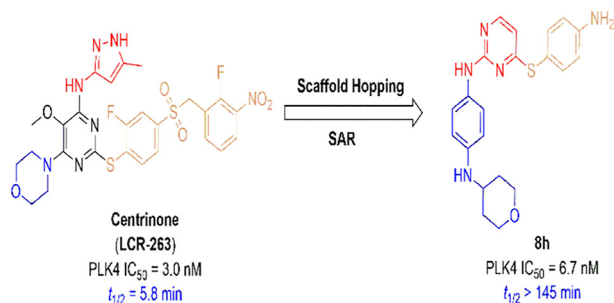
1778



Hybrid molecules of protoflavones and spirooxindole derivatives with selective cytotoxicity against triple-negative breast cancer cells

Gábor Girst, Elizabeth A. Lopes, Lídia M. Gonçalves, Margarida Espadinha, Norbert Kúsz, Hui-Chun Wang, Maria M. M. Santos* and Attila Hunyadi*

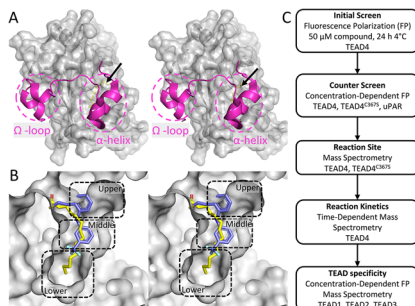
1787



Design, synthesis, and biological evaluation of novel pyrimidin-2-amine derivatives as potent PLK4 inhibitors

Yanli Xue, Shuyi Mu, Pengkun Sun, Yin Sun, Nian Liu, Yu Sun, Lin Wang, Dongmei Zhao* and Maosheng Cheng

1803

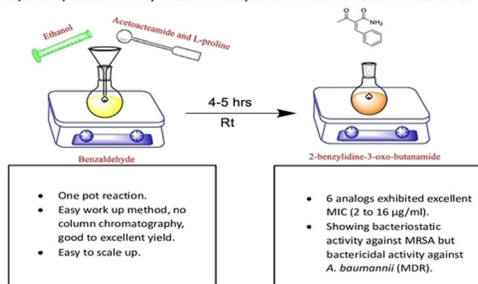


Chloroacetamide fragment library screening identifies new scaffolds for covalent inhibition of the TEAD-YAP1 interaction

Khuchtumur Bum-Erdene, Mona K. Ghosayel, Mark J. Zhang, Giovanni Gonzalez-Gutierrez and Samy O. Meroueh*

1817

Graphical representation of Synthesis of 2-benzylidene-3-oxobutanamide and its derivatives



Synthesis and antibacterial activity of 2-benzylidene-3-oxobutanamide derivatives against resistant pathogens

Ankur Sood and Venkitasamy Kesavan*

