

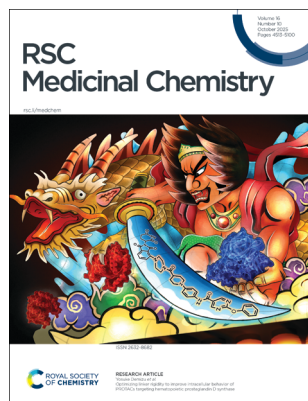
# RSC Medicinal Chemistry

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 16(10) 4513-5100 (2025)



### Cover

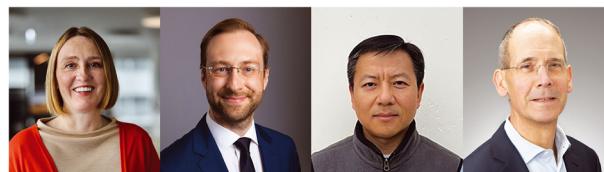
See Yosuke Demizu *et al.*,  
pp. 4721–4730.  
Image reproduced by  
permission of Yosuke Demizu  
from *RSC Med. Chem.*,  
2025, 16, 4721.

## EDITORIAL

4527

### Introduction to the themed collection on kinases

Meizhong Jin, Hayley Binch, David E. Heppner  
and Philip Jones



## OPINION

4528

### Emerging opportunities in the rewiring of biology through proximity inducing small molecules

Michael M. Hann





# RSC Advances

At the heart of open access for  
the global chemistry community

## Editor-in-chief

**Russell J Cox**

Leibniz Universität Hannover, Germany

## We stand for:



**Breadth** We publish work in all areas of chemistry and reach a global readership



**Quality** Research to advance the chemical sciences undergoes rigorous peer review for a trusted, society-run journal



**Affordability** Low APCs, discounts and waivers make publishing open access achievable and sustainable



**Community** Led by active researchers, we publish quality work from scientists at every career stage, and all countries

Submit your work now

[rsc.li/rsc-advances](https://rsc.li/rsc-advances)

@RSC\_Adv

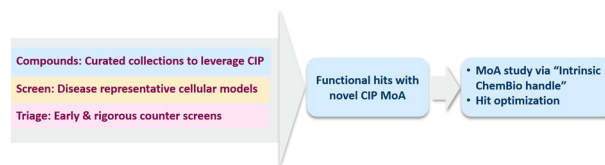


## REVIEWS

4532

## Target agnostic cellular screening in the era of chemically induced proximity

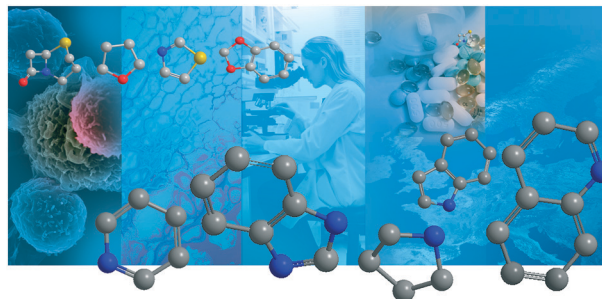
Meizhong Jin\*



4540

## Analysis of the structural diversity of heterocycles amongst European medicines agency approved pharmaceuticals (2014–2023)

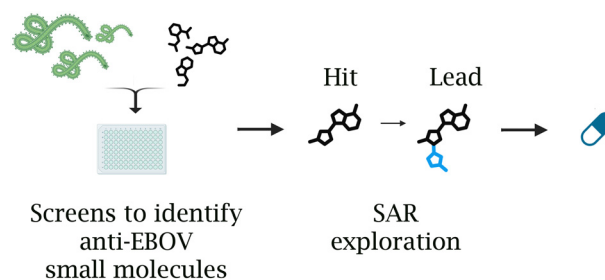
Matthew Ward and Niamh M. O'Boyle\*



4571

## Small molecule drug discovery for Ebola virus disease

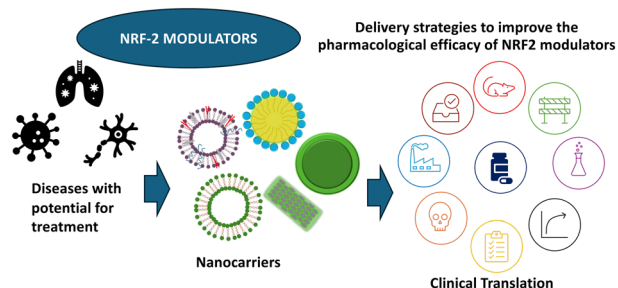
Destiny Durante, Venkatesh Murugesh, Tyler Kalanquin, Irina N. Gaisina, Lijun Rong and Terry W. Moore\*



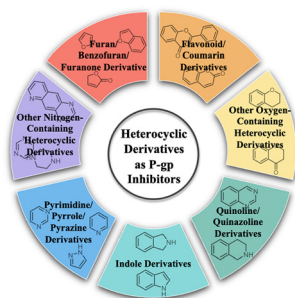
4599

## Delivery strategies to improve the pharmacological efficacy of NRF2 modulators: a review

Zerrin Sezgin Bayindir, Matej Sova, Nilufer Yuksel and Luciano Saso\*



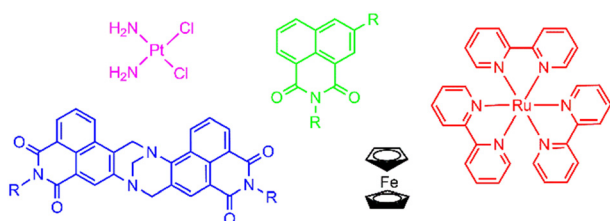
4617



### Development of heterocyclic derivatives as P-glycoprotein inhibitors against multidrug resistance: pharmacological activities, structure–activity relationship and target (2020–2024)

Zhikun Yang, Yanhong Yang, Zimeng Huang, Yi Hua, Mahmoud Emam Abd El-Salam Hassaan and Hong Wang\*

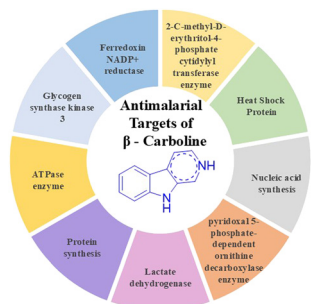
4657



### Naphthalimide–organometallic hybrids as multi-targeted anticancer and luminescent cellular imaging agents

David C. Magri\* and Alex D. Johnson

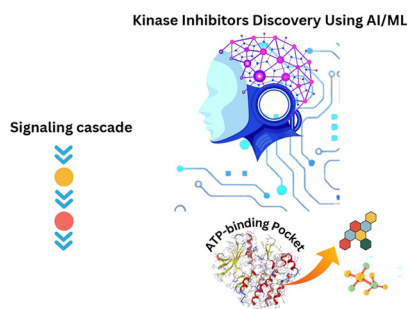
4676



### $\beta$ -Carboline: a privileged scaffold from nature for potential antimalarial activity

Amisha Punmiya, Alka Raj Pandey and Amisha Vora\*

4698



### Leveraging artificial intelligence and machine learning in kinase inhibitor development: advances, challenges, and future prospects

Mohamed S. Elgawish,\* Aya M. Almatary, Sawsan A. Zaitone and Mohamed S. H. Salem\*

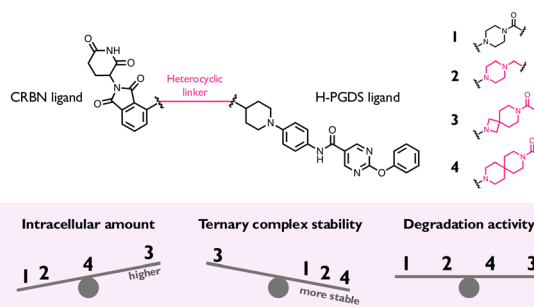


## RESEARCH ARTICLES

4721

### Optimizing linker rigidity to improve intracellular behavior of PROTACs targeting hematopoietic prostaglandin D synthase

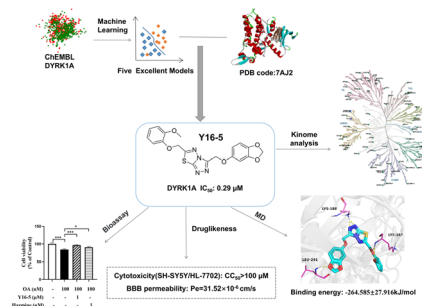
Hinata Osawa, Kosuke Saito and Yosuke Demizu\*



4731

### Computer-aided discovery of triazolothiadiazoles as DYRK1A-targeted neuroprotective agents

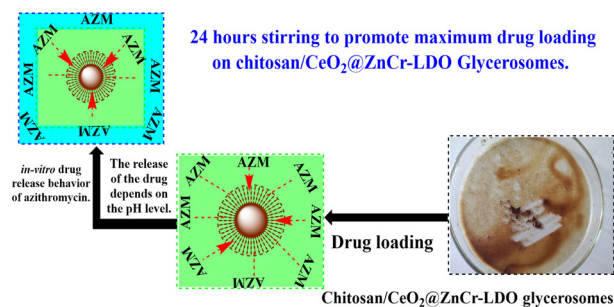
Xinxin Si, Yaling Wang, Nianzhuang Qiu, Chenliang Qian, Bochao Yang, Hongwei Jin, Hao Wang,\* Xuehui Zhang\* and Jie Xia\*



4742

### Design of chitosan-coated CeO<sub>2</sub>-doped ZnCr LDO nanocomposites for optimized azithromycin delivery: a kinetic and mechanistic perspective

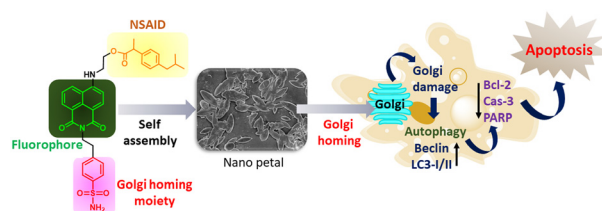
Hina Afzal, Muhammad Babar Taj,\* Merfat M. Alsabban, Walla Alelwani, Nadiyah Alahmadi, Noushi Zaidi, Nouf A. Babteen and Sana Afzal



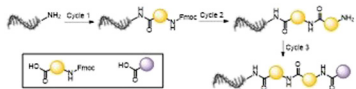
4767

### Routing NSAIDs into the Golgi apparatus induces autophagy and apoptosis in cancer cells

Aditi, Tripti Mishra, Asima Sahu, Unnati Modi, Dhiraj Bhatia and Sudipta Basu\*



4774



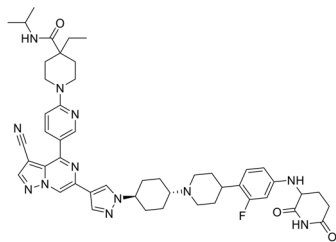
- 3 million-member library
- Lead-like properties
- High chemical diversity

## Design and synthesis of a chemically diverse, lead-like DNA-encoded library from sequential amide coupling

Cameron E. Taylor, Grace Roper, Rhianna Young, Fredrik Svensson, Andreas Brunschweiger, Sam Butterworth, Andrew G. Leach and Michael J. Waring\*

4781

Compound 20: An orally bioavailable, CNS active, pan-mutant RET Degrader

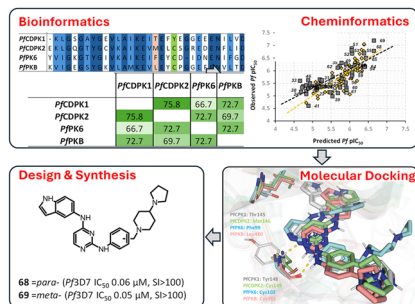


RET WT  $DC_{50}$  /  $E_{max}$  = 1.7 nM / 8%  
RET G810R  $DC_{50}$  /  $E_{max}$  = 21 nM / 22%

## Discovery of an orally bioavailable, CNS active pan-mutant RET kinase heterobifunctional degrader

D. L. Orsi, K. E. Lazarski, R. Improgo, R. V. Agafonov, J. Y. Ahn, J. Baddour, K. Cassidy, P. Chaturvedi, K. S. Cole, R. W. Deibler, W. A. Elam, M. E. Fitzgerald, V. J. Garza, A. Good, C. H. Hulton, M. Isasa, K. L. Jackson, P. Li, Y. Liang, R. E. Michael, M. W. O'Shea, M. Moustakim, S. Perino, F. Rahman, M. J. Schnaderbeck, N. P. Stone, B. Tillotson, G. K. Veits, A. Vogelaar, J. L. Yap, R. T. Yu, H. Huang and J. A. Henderson\*

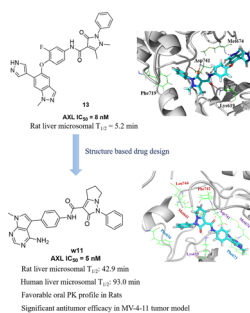
4796



## Computationally guided optimization of the antimalarial activity and physicochemical properties of 2,4-diaminopyrimidines

Guntur Guntur, Duangkamol Gleeson, Mark Anderson, Nicole Mutter, Lauren Webster, Kevin D. Read and M. Paul Gleeson\*

4818



## Structure-based drug discovery of novel penta- or hexa-bicyclo-pyrazolone derivatives as potent and selective AXL inhibitors

Mingming Sun, Shuang Wu, Ning Xi\* and Qianying Cao\*

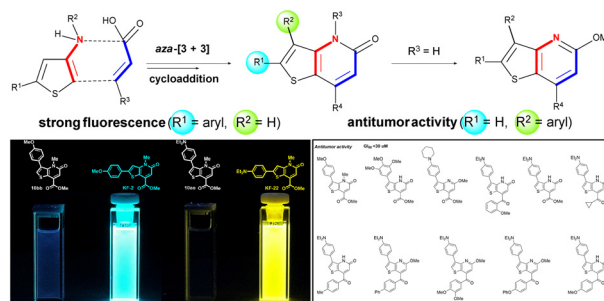


## RESEARCH ARTICLES

4837

Site-dependent modulation of antitumor activity and fluorescence in thieno[3,2-*b*]pyridin-5(4*H*)-ones

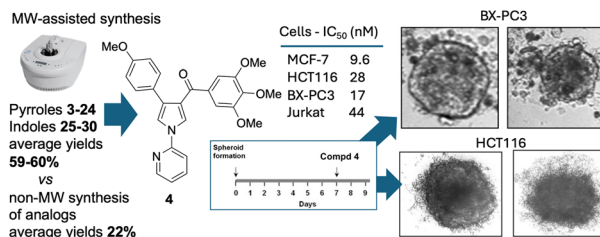
Dan-Bi Sung, Pham Van Thong, Jieun Yun, Joo-Hee Kwon, Sol Park, Sang Kook Woo, Jong Soon Kang and Jong Seok Lee\*



4845

## Microwave-assisted synthesis of tubulin assembly inhibitors as anticancer agents by aryl ring reversal and conjunctive approach

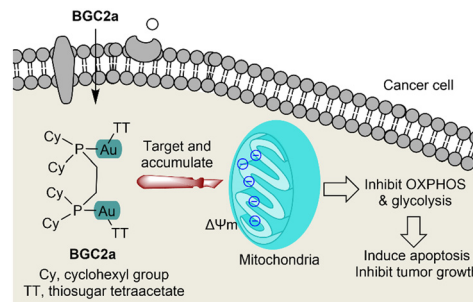
Domiziana Masci, Michela Puxeddu, Claudia Colla, Antonio Coluccia, Martina Santelli, Pietro Sciò, Elena Mariotto, Giampietro Viola, Ernest Hamel, Rosa Lerose, Carmela Mazzoccoli, Romano Silvestri\* and Giuseppe La Regina



4859

## Investigation of the anticancer efficacy and impact on energy metabolism of dual-core gold(i) complex BGC2a

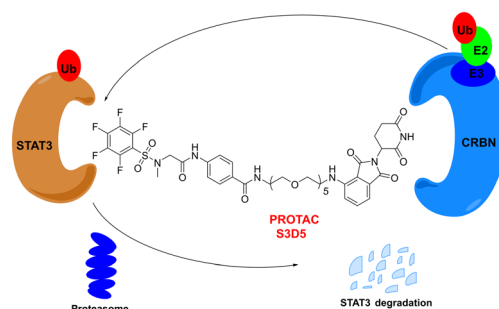
Hai-Ling Gao, Wenwen Ding, Zhi-Xin Shen\* and Qingbin Cui\*



4872

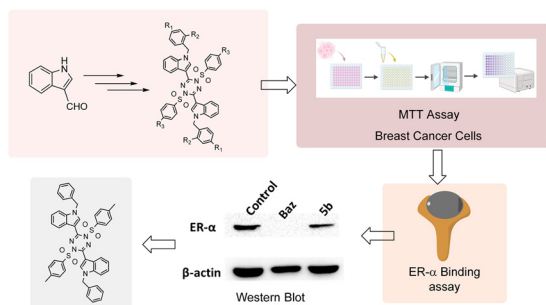
## Discovery of a potent and selective PROTAC degrader for STAT3

Kefeng Wang, Yuxin Zheng, Wenli Mao, Jing Xu\* and Yukun Wang\*



## RESEARCH ARTICLES

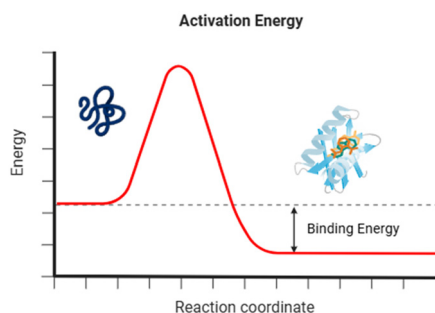
4878



### Design, synthesis and biological evaluation of novel bis(indolyl)-tetrazine derivatives as anti-breast cancer agents

Kamalpreet Kaur, Harkomal Verma, Prabhakar Gangwar, Monisha Dhiman and Vikas Jaitak\*

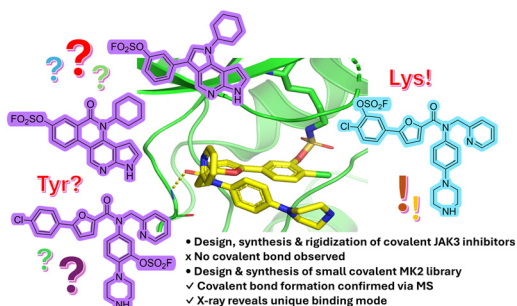
4892



### Thermodynamics and mechanism of afatinib-EGFR binding through a QM/MM approach

Anjali Kisku, Raghav Wahi and Raj Kumar Mishra\*

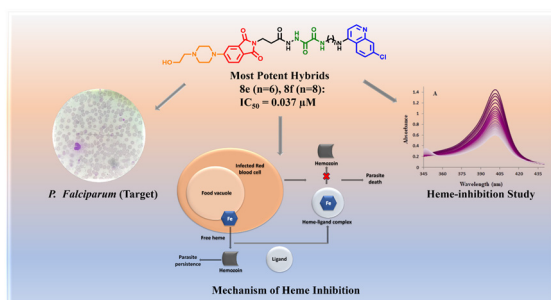
4906



### A twist in the tale: shifting from covalent targeting of a tyrosine in JAK3 to a lysine in MK2

Laura Hillebrand, Guiqun Wang, Alexander Rasch, Benedikt Masberg, Apirat Chaikuad, Thales Kronenberger, Ellen Günther, Michael Forster, Antti Poso, Michael Lämmerhofer, Stefan A. Laufer, Stefan Knapp and Matthias Gehring\*

4920



### Design, synthesis, and anti-plasmodial profiling of oxalamide-linked 4-aminoquinoline-phthalimide hybrids

Nikita Gupta, Kewal Kumar, Raghu Raj\* and Vipran Kumar\*

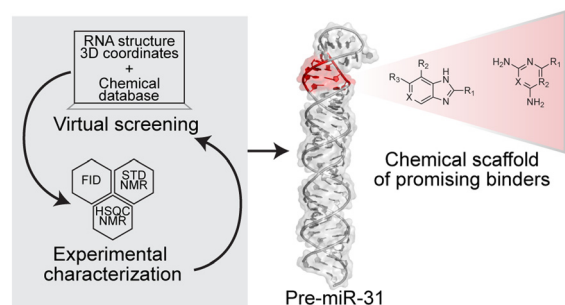


## RESEARCH ARTICLES

4929

### Integrated *in silico* and experimental screening identifies novel ligands that target precursor microRNA-31 at the dicer cleavage site

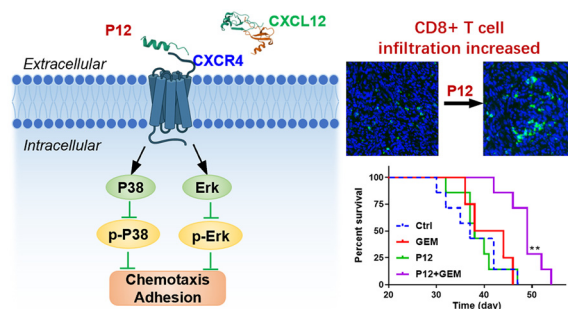
Grace Arhin, Lily Haghpassand and Sarah C. Keane\*



4940

### Development of a CXCR4 antagonistic peptide, P12, to suppress pancreatic cancer progress *via* enhancing T cell responses and sensitizing cells to gemcitabine

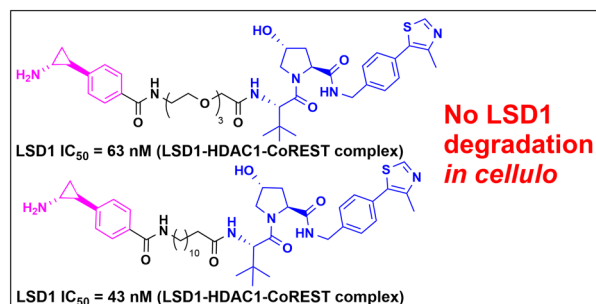
Xin Huang, Hang Wu, Ke Zhu, Xuanxin Liu, Dapeng Li, Yuanhao Liu, Tao Wang, Tao Wen, Xiaocui Fang, Jian Liu, Yanlian Yang, Jie Meng,\* Chen Wang\* and Haiyan Xu\*



4952

### Synthetic and structure–activity studies of SP2577 and TCP towards LSD1 targeting PROTACs

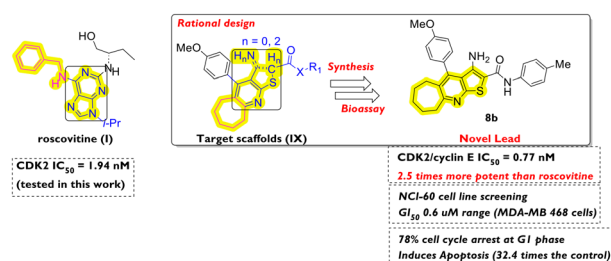
Megan E. Coulson, James K. S. Norris, Sean A. Smith, Joshua P. Smalley, John W. R. Schwabe,\* Shaun M. Cowley\* and James T. Hodgkinson\*



4960

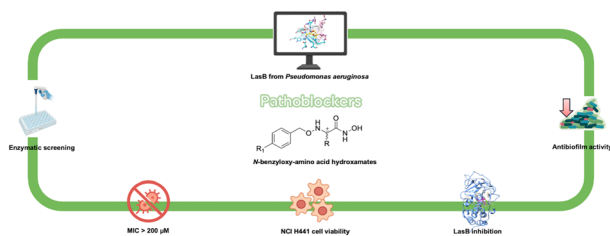
### CDK2 inhibitors: rationally directed discovery of a novel potent lead derived from cyclohepta[e]thieno[2,3-*b*]pyridine

Omaima F. Ibrahim, Raed M. Maklad,\* Hajjaj H. M. Abdu-Allah, Yasmin M. Syam and Etify A. Bakhite\*



## RESEARCH ARTICLES

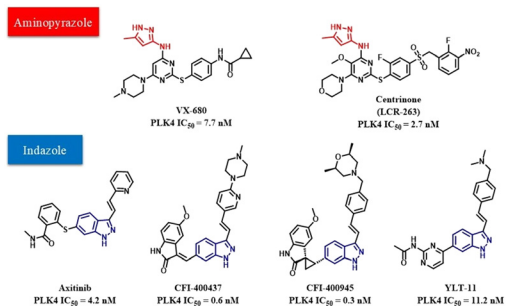
4973



### Identification of novel *N*-benzyloxy-amino acid hydroxamates as inhibitors of the virulence factor LasB from *Pseudomonas aeruginosa*

Riccardo Di Leo, Enrico Crispino, Doretta Cuffaro, Giuseppantonio Maisetta, Andrea Bertacca, Marta Bianchi, Giovanna Batoni, Imin Wushur, Fatema Amatur Rahman, Jan-Olof Winberg, Ingebrigt Sylte, Armando Rossello and Elisa Nuti\*

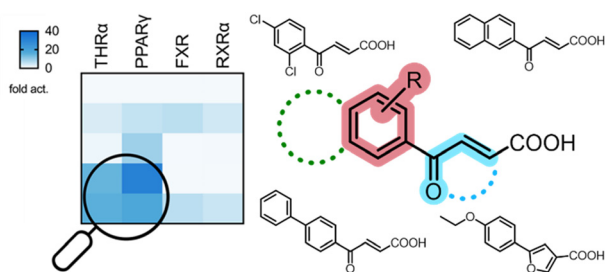
4997



### Design, synthesis, and biological evaluation of 5-chlorine-2-amino-pyrimidine derivatives as potent PLK4 inhibitors

Shuyi Mu, Wenqiang Sun, Zehui Qi, Minghui Tong, Xuan Shi, Han Wang, Nian Liu, Pengkun Sun, Cunzheng Fan, Ningyuan Hu, Yixiang Sun, Haoyu Zhang, Zixuan Gao, Dongmei Zhao\* and Maosheng Cheng

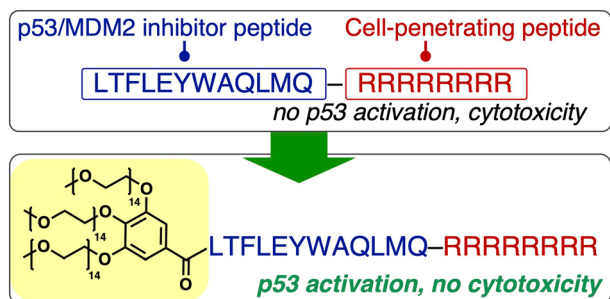
5012



### Fragment-based discovery of dual ligand pharmacophores for lipid-sensing transcription factors for designed polypharmacology

Tanja Stiller, Silke Duensing-Kropp, Julian A. Marschner and Daniel Merk\*

5025



### Polyethylene glycol incorporation to reduce the cytotoxicity associated with cationic cell-penetrating-peptide conjugation

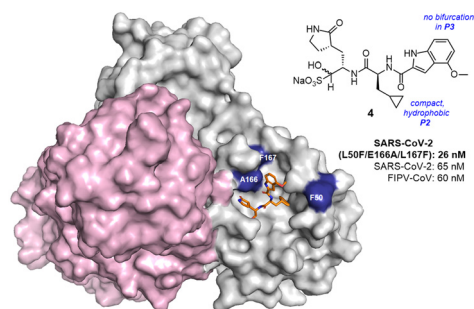
Naoki Umezawa,\* Kazuma Arakawa, Maiko Kato, Yosuke Hisamatsu, Hirokazu Yagi, Chiharu Miyajima and Yasumichi Inoue



5032

### Structural insights into the nirmatrelvir-resistant SARS-CoV-2 M<sup>PTO</sup> L50F/E166A/L167F triple mutant-inhibitor-complex reveal strategies for next generation coronaviral inhibitor design

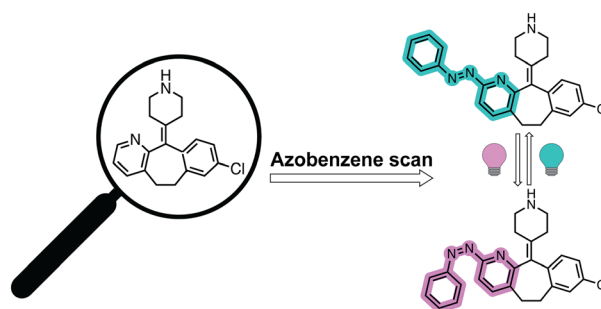
Conrad Fischer, Jimmy Lu, Marco J. van Belkum, Sydney Demmon, Pu Chen, Chaoxiang Wang, Tayla J. Van Oers, Tess Lamer, M. Joanne Lemieux and John C. Vederas\*



5041

### Design and synthesis of photoswitchable desloratadine ligands for histamine H<sub>1</sub> receptor photopharmacology

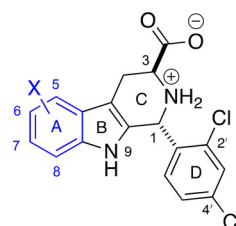
Lars C. P. Binkhorst, Ivana Josimovic, Daan de Vetten, Tyrone J. Nijman, Niels J. Hauwert, Sufyan Ahmad, Oscar P. J. van Linden, Iwan J. P. de Esch, Henry F. Vischer, Maikel Wijtmans\* and Rob Leurs\*



5052

### Benzo-ring modification on Malaria Box hit MMV008138: effects on antimalarial potency and microsomal stability

Maryam Ghavami, Haibo Li, Lixuan Liu, Joshua H. Butler, Sha Ding, Grant J. Butschek, Reagan S. Haney, R. McAlister Council-Troche, R. Justin Grams, Emilio F. Merino, Jennifer M. Davis, Maxim Totrov, Maria B. Cassera and Paul R. Carlier\*



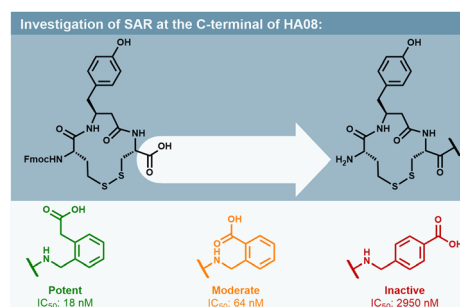
19 A-ring substitutions explored; only 3 showed antimalarial potency within 3-fold of the parent. F is tolerated, CN and larger groups are not.

	X	EC <sub>50</sub> (nM)	mouse microsomal t <sub>1/2</sub>
1	H	250 ± 70	~10 min
20a	5-F	451 ± 28	~10 min
20c	7-F	501 ± 47	<b>214 min</b>
20d	8-F	717 ± 73	15 min

5059

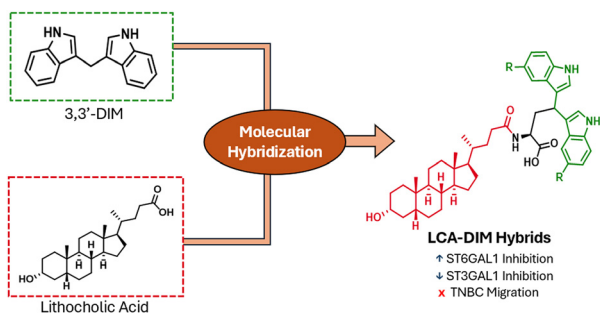
### Novel macrocyclic peptidomimetics targeting the insulin-regulated aminopeptidase (IRAP): design, synthesis and evaluation

Esther Olaniran Håkansson, Lorenzo J. I. Balestri, Sharathna Puthiyaparambath, Sebastian Moes, Henning Henschel, Christian Sköld, Mathias Hallberg, Mats Larhed, Bobo Skillinghaug and Luke R. Odell\*



## RESEARCH ARTICLES

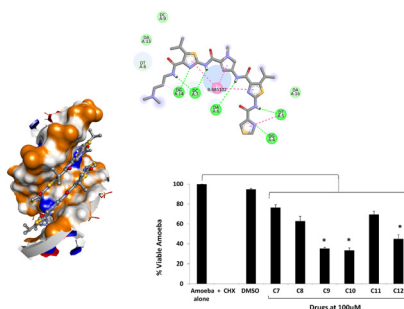
5070



### Novel lithocholic acid-diindolylmethane hybrids as potent sialyltransferase inhibitors targeting triple-negative breast cancer: a molecular hybridization approach

Christian Angelo P. Concio, Ser John Lynon P. Perez, Tzu-Ting Chang, Chia-Ling Chen, Yi-Ting He, Susan D. Arco\* and Wen-Shan Li\*

5084



### Exploring novel thiazole-based minor groove binding agents as potential therapeutic agents against pathogenic *Acanthamoeba castellanii*

Hasan Y. Alniss,\* Ruqaiyyah Siddiqui, Meshal Daalah, Hadeel M. Al-Jubeh, Yousef A. Msallam, Bader S. Alawfi, Sreedevi Sajeev, Anil Ravi and Naveed A. Khan\*

## CORRECTION

5097

### Correction: Emerging opportunities in the rewiring of biology through proximity inducing small molecules

Michael M. Hann

