

# RSC Medicinal Chemistry

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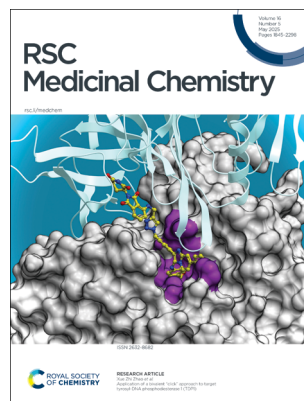
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## IN THIS ISSUE

ISSN 2632-8682 CODEN RMCSCX 16(5) 1845-2298 (2025)



**Cover**  
See Constantin Mamat *et al.*, pp. 1856–1864.  
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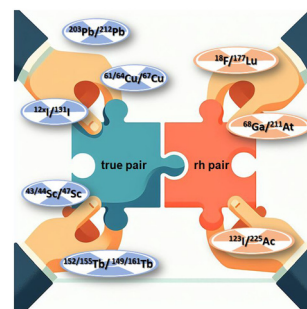
**Inside cover**  
See Xue Zhi Zhao *et al.*, pp. 1969–1985.  
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## REVIEWS

1856

### Enhancing the radionuclide theranostic concept through the radiohybrid approach

Tobias Krönke, Klaus Kopka and Constantin Mamat\*

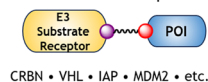


1865

### Small molecule targeted protein degradation *via* the UPS: venturing beyond E3 substrate receptors

Renyu Guo, Fukang Yang and Emily C. Cherney\*

Traditional TPD approaches co-opting E3 substrate receptors:



Nascent TPD approaches co-opting alternative UPS components:



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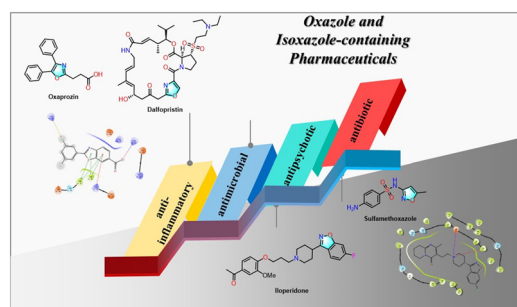


## REVIEWS

1879

## Oxazole and isoxazole-containing pharmaceuticals: targets, pharmacological activities, and their SAR studies

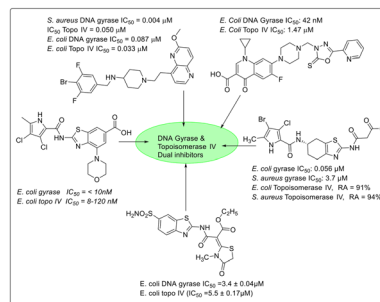
Shanshan Li, Yiou Mei, Luchen Jiang, Xueyan Yang, Wei Zeng and Yunfei Du\*



1891

## Recent advancements in the development of next-generation dual-targeting antibacterial agents

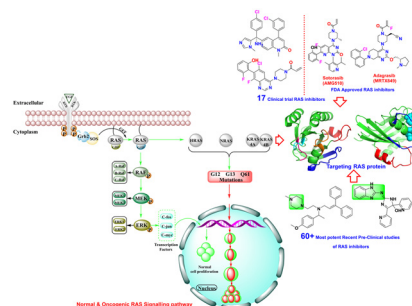
Firdoos Ahmad Sofi,\* Mayank, Mubashir H. Masoodi and Nahida Tabassum



1923

## Structural insights, regulation, and recent advances of RAS inhibitors in the MAPK signaling cascade: a medicinal chemistry perspective

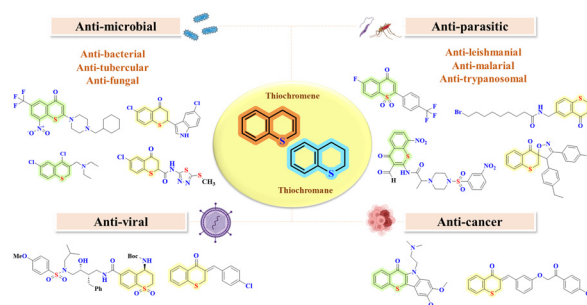
Vineet Prajapati, Ankit Kumar Singh, Adarsh Kumar, Harshwardhan Singh, Prateek Pathak, Maria Grishina, Vikas Kumar, Habibullah Khalilullah, Amita Verma and Pradeep Kumar\*



1941

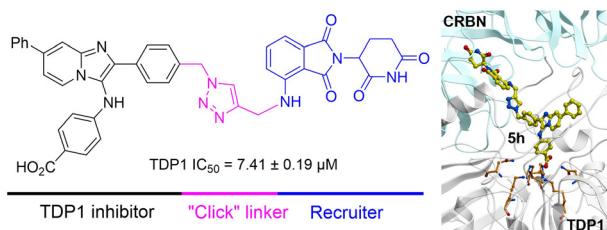
## Thiochromenes and thiochromanes: a comprehensive review of their diverse biological activities and structure–activity relationship (SAR) insights

Jatin, Solai Murugappan, Shivani Kirad, Chandu Ala, Pranali Vijaykumar Kuthe, Chandra Sekhar Venkata Gowri Kondapalli and Murugesan Sankaranarayanan\*



## RESEARCH ARTICLES

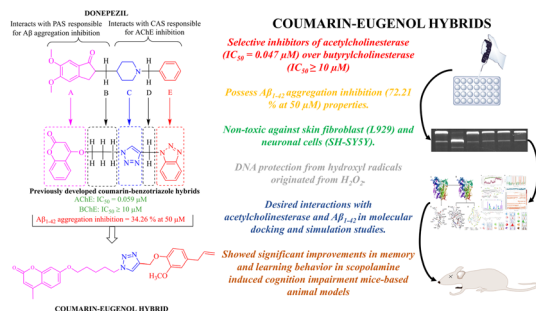
1969



## Application of a bivalent "click" approach to target tyrosyl-DNA phosphodiesterase 1 (TDP1)

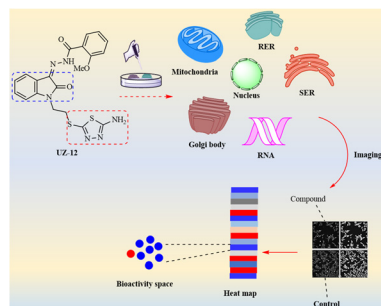
Xue Zhi Zhao,\* Wenjie Wang, Md Rasel Al Mahmud, Keli Agama, Yves Pommier and Terrence R. Burke Jr.

1986

Development of coumarin-inspired bifunctional hybrids as a new class of anti-Alzheimer's agents with potent *in vivo* efficacy

Atamjit Singh,\* Aman Sharma, Karanvir Singh, Kirandeep Kaur, Pallvi Mohana, Jignesh Prajapati, Uttam Kaur, Dweepayan Goswami, Saroj Arora, Renu Chadha and Preet Mohinder Singh Bedi\*

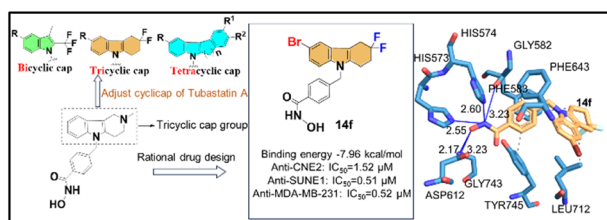
2004



## Identification of 5-amino-1,3,4-thiadiazole appended isatins as bioactive small molecules with polypharmacological activities

Uzma Azam, Waqar Ahmed Humayun, Amrutha K. Avathan Veetil, Yang Liu, Oguz Hastürk, Mao Jiang, Sonja Sievers, Peng Wu\* and Muhammad Moazzam Naseer\*

2019

Synthesis of fluorinated tubastatin A derivatives with bi-, tri-, and tetracyclic cap groups: molecular docking with HDAC6 and evaluation of *in vitro* antitumor activity

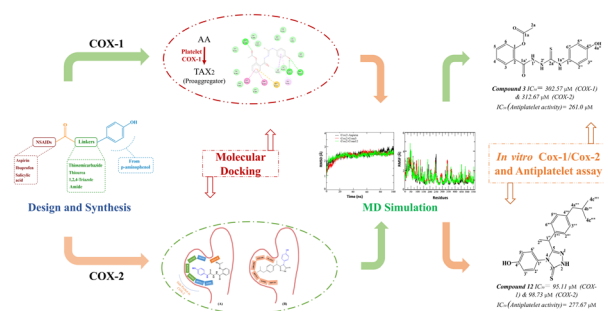
Huaxin Luo, Zheng Huang, Xiangdong Mo, Chunmei Long, Kaiyuan Wang, Rong Deng,\* Xiaofeng Zhu\* and Zhuo Zeng\*



2027

## Aspirin vs. ibuprofen: unveiling the distinct cyclooxygenase-1/2 behaviour and dual efficacy of their synthesized analogues *via* molecular modeling and *in vitro* biological assessment

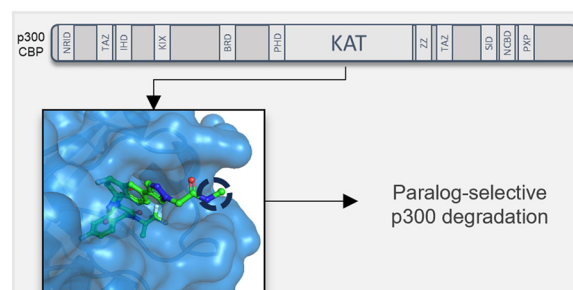
Amandeep Kaur, Hafiz Muzzammel Rehman, Vipin Kumar Mishra, Gurmeet Kaur, Mandeep Kaur, Mohammad K. Okla, Masaud Shah and Manisha Bansal\*



2049

## Development of p300-targeting degraders with enhanced selectivity and onset of degradation

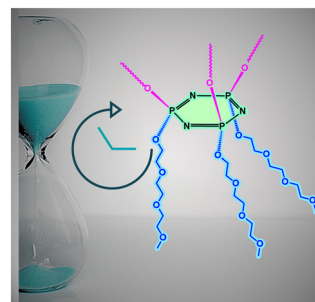
Graham P. Marsh, Mark S. Cooper, Sean Goggins, Stephen J. Reynolds, Dean F. Wheeler, Joel O. Cresser-Brown, Robert E. Arnold, Emily G. Babcock, Gareth Hughes, Darko Bosnakovski, Michael Kyba, Samuel Ojeda, Drew A. Harrison, Christopher J. Ott and Hannah J. Maple\*



2061

## Design, synthesis and *in vitro* evaluations of new cyclotriphosphazenes as safe drug candidates

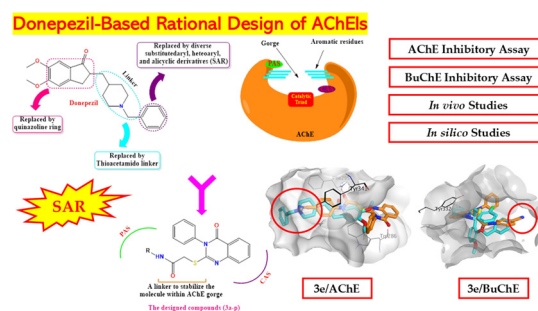
Elif Yıldız Gül, Büşra Tiryaki, Buse Köse, Nuri Öztürk, Elif Okutan, Burcu Dedeoğlu and Esra Tanrıverdi Eçik\*



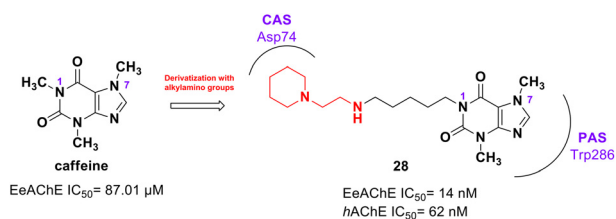
2078

## Donepezil-based rational design of *N*-substituted quinazolinthioacetamide candidates as potential acetylcholine esterase inhibitors for the treatment of Alzheimer's disease: *in vitro* and *in vivo* studies

Ahmed A. Al-Karmalawy,\* Ahmed F. Mohamed, Heba Nasr Shalaby, Ayman Abo Elmaaty, Riham A. El-Shiekh, Mohamed A. Zeidan, Radwan Alnajjar, Abdullah Yahya Abdullah Alzahrani, Mohammed H. AL Mughram, Moataz A. Shaldam and Haytham O. Tawfik\*



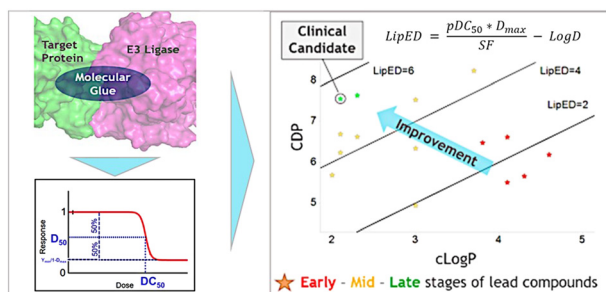
2098



### Novel potent and selective dual acetylcholinesterase inhibitors: *N*-substituted theobromine and theophylline derivatives

Brunella Biscussi,\* Eduardo J. Cueto-Díaz, Concepción Pérez, María Isabel Rodríguez-Franco and Ana Paula Murray\*

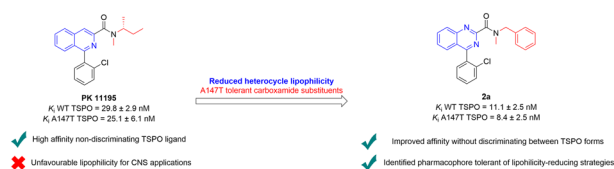
2117



### Leveraging efficiency metrics for the optimization of CELMoDs™ as cereblon-based molecular glue degraders

Lei Jia, Jennifer R. Riggs, Dahlia R. Weiss, Brian L. Claus, Veerabahu Shanmugasundaram, Stephen R. Johnson and Christoph W. Zapf\*

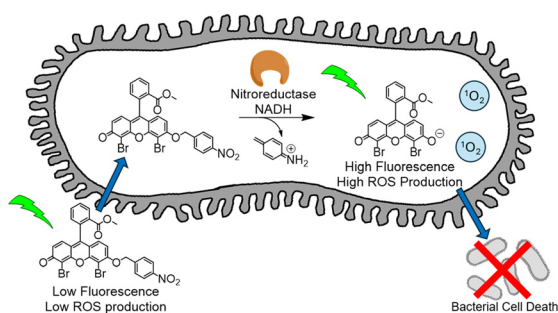
2124



### PK 11195 derivatives: exploring the influence of amide and heterocyclic substitution on A147T TSPO discrimination

Renee Sokias, Andrea Zhao, Eryn L. Werry, Andrew P. Montgomery, David E. Hibbs, Michael A. Sullivan, André D. J. McKenzie, Grace A. Cumbers, Beau M. Allen, Jonathan J. Danon and Michael Kassiou\*

2133



### Nitroreductase-activatable photosensitizers for selective antimicrobial photodynamic therapy

Matthew T. Tung, Tianyi Ma, Ivonne Rebeca Lopez-Miranda, Joshua N. Milstein\* and Andrew A. Beharry\*

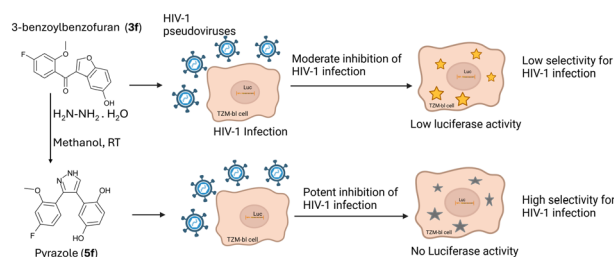


## RESEARCH ARTICLES

2142

### The synthesis and investigation of novel 3-benzoylbenzofurans and pyrazole derivatives for anti-HIV activity

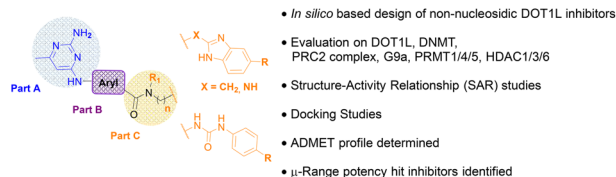
Sinothile S. Khuzwayo, Mamoalosi A. Selepe, Debra Meyer and Ntombenhle H. Gama\*



2159

### Design, synthesis and evaluation of pyrimidinobenzylamide and pyrimidinothiophenamide derivatives as inhibitors of DOT1L and related epigenetic targets DNMT3a, PRMT4 and other HMTs

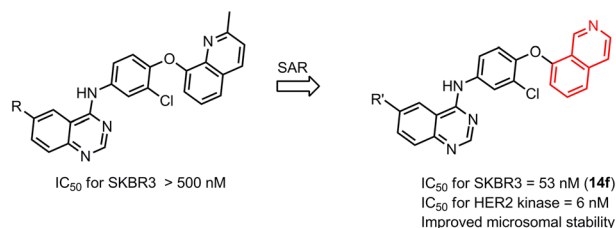
Oscar Omar Castillo-Aguilera,\* Patrick Depreux, Ludovic Halby, Christian Bailly, Lenin Domínguez-Ramírez, Sheraz Gul, Paola B. Arimondo and Laurence Goossens\*



2174

### Discovery of isoquinoline-tethered quinazoline derivatives with enhanced HER2 inhibition over EGFR

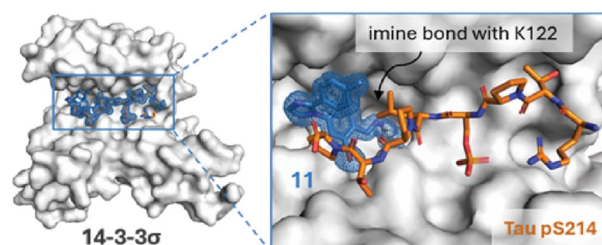
Jung Wuk Lee, Chang Gyun Im, Ji Min Lee, Minsang Cho, Mingi Kim, Kiho Lee, Hien Thi Thu Nguyen, Jiwon Seo, Ji Hae Seo and Kyung Hoon Min\*



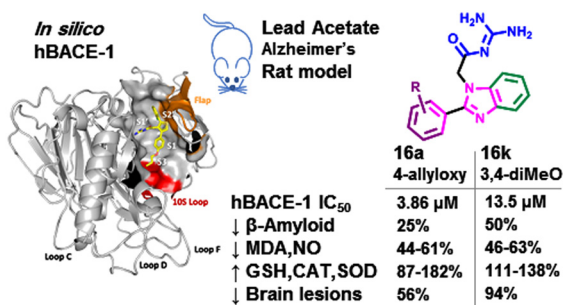
2190

### Site-specific molecular glues for the 14-3-3/Tau pS214 protein-protein interaction via reversible covalent imine tethering

Ansgar Oberheide, Maxime C. M. van den Oetelaar, Jakob J. A. Scheele, Jan Borggräfe, Semmy F. H. Engelen, Michael Sattler, Christian Ottmann,\* Peter J. Cossar and Luc Brunsveld\*



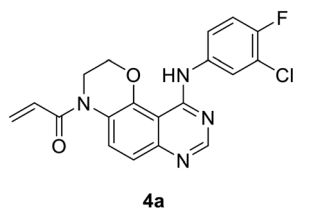
2202



### Development, biological evaluation, and molecular modelling of novel isocytosine and guanidine derivatives as BACE1 inhibitors using a fragment growing strategy

Asmaa M. Atta, Nouran Rihan, Ahmad M. Abdelwaly, Mohamed S. Nafie, Mohamed S. Elgawish, Samia M. Moustafa, Mohamed A. Helal and Khaled M. Darwish\*

2231

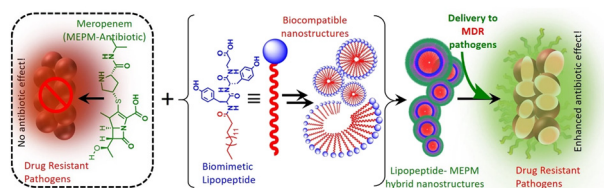


EGFR <sup>wt</sup>	IC <sub>50</sub> = 12.36 nM
H1975 cells	IC <sub>50</sub> = 0.63 μM
H1563 cells	IC <sub>50</sub> > 40 μM

### Design, synthesis and biological evaluation of 2H-[1,4]oxazino-[2,3-f]quinazolin derivatives as potential EGFR inhibitors for non-small cell lung cancer

Linchang Huang, Ying Zhang, Peng Liu, Lihong Lan, Lifang Yang, Bo Wang, Tingting Cao, Liming Hu and Xuemei Qin\*

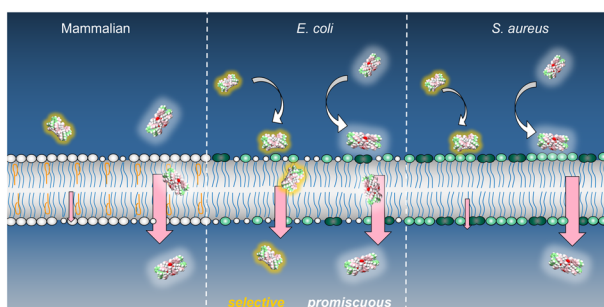
2240



### Self-responsive biomimetic short lipopeptide-based delivery systems for enhanced antibiotic efficacy against drug-resistant infections

Shruti Sharma, Deepanshi Saxena, Aanand Kautu, Sidharth Chopra\* and Khashti Ballabh Joshi\*

2249



### Membrane lipid composition directs the cellular selectivity of antimicrobial metallohelices

Nicola J. Rogers,\* Miles L. Postings, Ann M. Dixon, John Moat, Georgia Shreeve, Louise Stuart, Nicholas R. Waterfield and Peter Scott

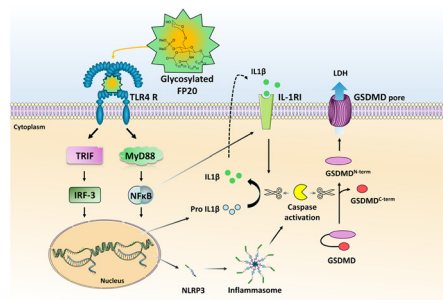


## RESEARCH ARTICLES

2261

### Towards more efficient synthetic immunomodulators: biological characterization and mechanism of action of monosaccharide-derived TLR4 agonists

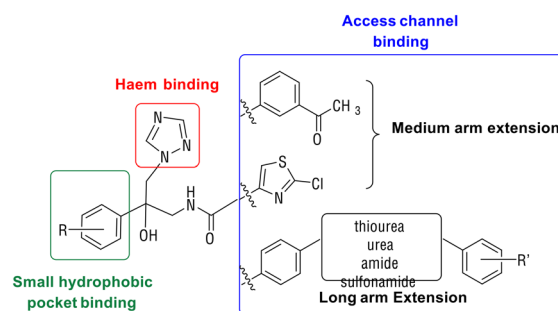
Ana Rita Franco, Zaineh Aladailleh, Alessio Romerio, Alice Italia, Federico Lami, Mohammed Monsoor Shaik, Natalia Skupinska, Valentina Artusa, Grisha Pirianov and Francesco Peri\*



2270

### Exploring medium and long arm extensions of 1,2,4-triazole derivatives as *Candida albicans* 14 $\alpha$ -demethylase (CYP51) inhibitors

Marwa Alsulaimany, Faizah A. Binjubair, Esra Tatar, Diane E. Kelly, Steven L. Kelly, Andrew G. Warrilow, Mikhail V. Keniya, Brian C. Monk, Josie E. Parker\* and Claire Simons\*



2281

### Design, synthesis and evaluation of acetylcholine-antitumor lipid hybrids led to identification of a potential anticancer agent disrupting the CDK4/6-Rb pathway in lung cancer

Ahmed H. E. Hassan, Eun Seo Bae, Youngdo Jeong, Chae Won Ock, Selwan M. El-Sayed, Minji Kim, Mohamed F. Radwan, Tarek S. Ibrahim, Jun-Young Cho, Boyoung Y. Park, Jaehoon Sim, Sang Kook Lee\* and Yong Sup Lee\*

