ELSEVIER

Bioorganic & Medicinal Chemistry Letters

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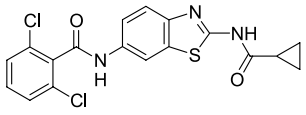
Contents

ARTICLES

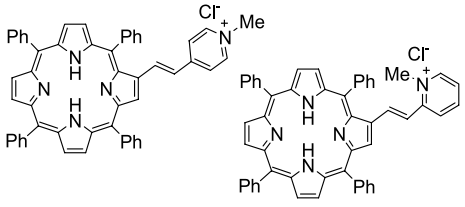
Synthesis and biological evaluation of benzothiazole derivatives as potent antitumor agents pp 3328–3332
Masao Yoshida, Ichiro Hayakawa, Noriyuki Hayashi, Toshinori Agatsuma, Youko Oda, Fumie Tanzawa, Shiho Iwasaki, Kumiko Koyama, Hidehiko Furukawa, Shinichi Kurakata and Yuichi Sugano*



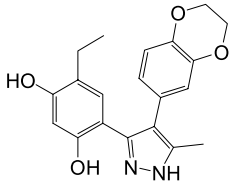
EC_{50} = 13 ng/mL

A compound library for structure optimization was synthesized to find out highly potent agents. The selected derivatives exhibited excellent in vivo inhibitory effect on tumor growth.

Synthesis of cationic β-vinyl substituted *meso*-tetraphenylporphyrins and their in vitro activity against herpes simplex virus type 1 pp 3333–3337
Eduarda M. P. Silva, Francesca Giuntini, Maria A. F. Faustino, João P. C. Tomé, Maria G. P. M. S. Neves, Augusto C. Tomé, Artur M. S. Silva, Maria G. Santana-Marques, António J. Ferrer-Correia, José A. S. Cavaleiro,* Maria F. Caeiro, Ricardo R. Duarte, Sabina A. P. Tavares, Inês N. Pegado, Bruno d'Almeida, António P. A. De Matos and Maria L. Valdeira

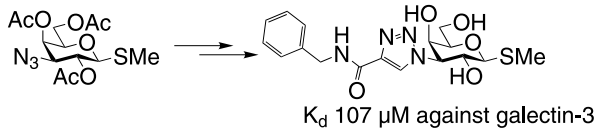


The identification, synthesis, protein crystal structure and in vitro biochemical evaluation of a new 3,4-diarylpyrazole class of Hsp90 inhibitors pp 3338–3343
Kwai-Ming J. Cheung, Thomas P. Matthews, Karen James, Martin G. Rowlands, Katherine J. Boxall, Swee Y. Sharp, Alison Maloney, S. Mark Roe, Chrisostomos Prodromou, Laurence H. Pearl, G. Wynne Aherne, Edward McDonald* and Paul Workman

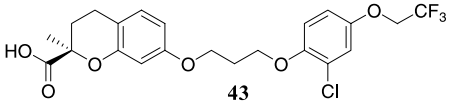


CCT018159
IC_{50} = 7.1μM, GI_{50} = 4.1μM

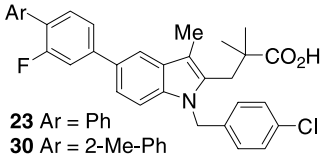
3-(1,2,3-Triazol-1-yl)-1-thio-galactosides as small, efficient, and hydrolytically stable inhibitors of galectin-3 pp 3344–3346
Bader A. Salameh, Hakon Leffler and Ulf J. Nilsson*



(2*R*)-2-Methylchromane-2-carboxylic acids: Discovery of selective PPARα agonists as hypolipidemic agents pp 3347–3351
Hiroo Koyama,* Julia K. Boueres, Daniel J. Miller, Joel P. Berger, Karen L. MacNaul, Pei-ran Wang, Marc C. Ippolito, Samuel D. Wright, Arun K. Agrawal, David E. Moller and Soumya P. Sahoo*

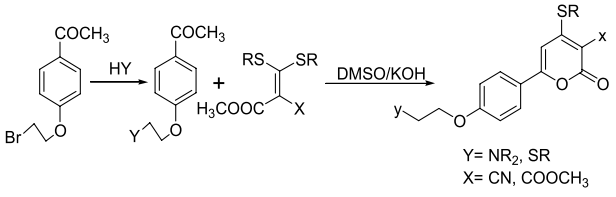


Inhibitors of the inducible microsomal prostaglandin E_2 synthase (mPGES-1) derived from MK-886 pp 3352–3355
Denis Riendeau,* Renee Aspiotis, Diane Ethier, Yves Gareau, Erich L. Grimm, Jocelyne Guay, Sébastien Guiral, Hélène Juteau, Joseph A. Mancini, Nathalie Méthot, Joel Rubin and Richard W. Friesen

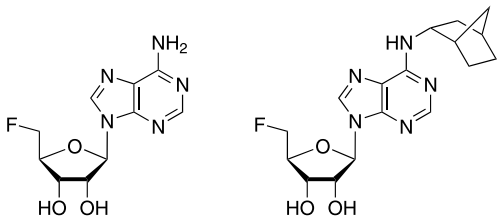


The in vitro potency and selectivity of a novel series of mPGES-1 inhibitors derived from MK-886 is described. SAR studies in this series led to the identification of inhibitors **23** and **30**.

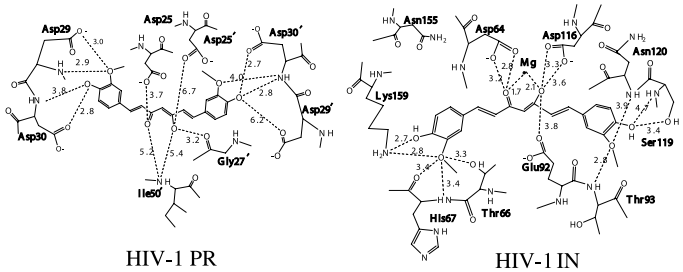
6-Aryl-4-methylsulfanyl-2*H*-pyran-2-one-3-carbonitriles as PPAR-γ activators pp 3356–3360
Ashoke Sharon, Ramendra Pratap, Rit Vatsyayan, Prakas R. Maulik, Uma Roy, Atul Goel and Vishnu Ji Ram*



An improved synthesis of 5′-fluoro-5′-deoxyadenosines **pp 3361–3363**
Trent D. Ashton and Peter J. Scammells*



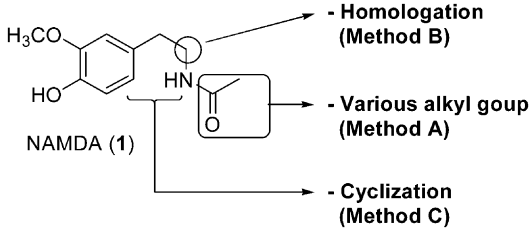
Active site binding modes of curcumin in HIV-1 protease and integrase **pp 3364–3368**
Opa Vajragupta,* Preecha Boonchoong, Garrett M. Morris and Arthur J. Olson



HIV-1 PR HIV-1 IN

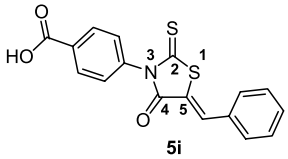
Computational docking of curcumin with HIV-1 integrase (IN) and protease (PR) is reported.

Syntheses of NAMDA derivatives inhibiting NO production in BV-2 cells stimulated with lipopolysaccharide **pp 3369–3373**
Jai Woong Seo, Ekaruth Srisook, Hyo Jin Son, Onyou Hwang,* Young-Nam Cha and Dae Yoon Chi*



Sixteen derivatives of NAMDA (**1**), an inhibitor of BH_4 synthesis, were designed and synthesized.

Rhodanine derivatives as inhibitors of JSP-1 **pp 3374–3379**
Neil S. Cutshall,* Christine O'Day and Marina Prezhdo

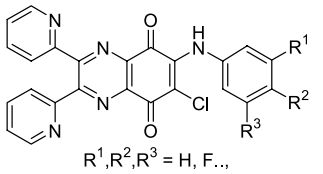


5i

IC_{50} 18 μM

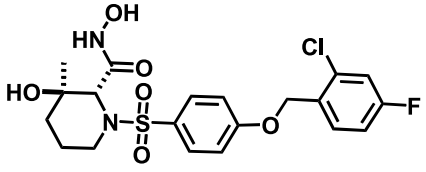
A series of rhodanine-based inhibitors was synthesized and shown to be novel, potent, and selective inhibitors against JNK-stimulating phosphatase-1 (JSP-1), a member of the dual-specificity phosphatase family.

Synthesis and biological evaluation of quinoxaline-5,8-diones that inhibit vascular smooth muscle cell proliferation pp 3380–3384
Hwa-Jin Chung, Ok-Jai Jung, Mi Jin Chae, Sung-Yu Hong, Kwang-Hoe Chung, Sang Kook Lee and Chung-Kyu Ryu*

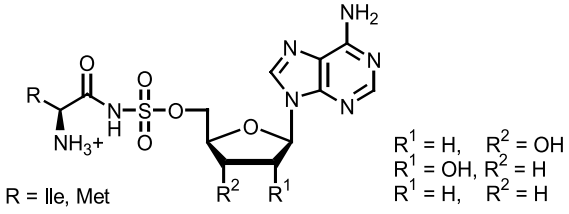


6-Arylamino-2,3-bis(pyridin-2-yl)-7-chloro-quinoxaline-5,8-diones were synthesized and evaluated for their antiproliferative activity on rat aortic smooth muscle cells. The quinoxaline-5,8-diones exhibited a potent antiproliferative activity.

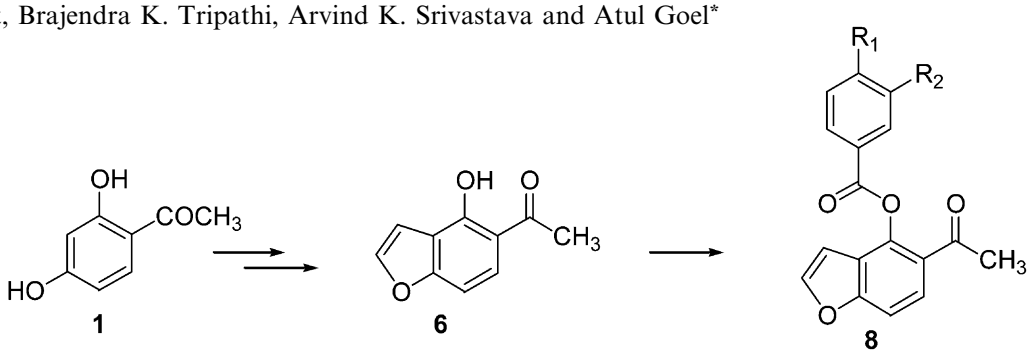
Discovery of 3-OH-3-methylpipecolic hydroxamates: Potent orally active inhibitors of aggrecanase and MMP-13 pp 3385–3388
Mark C. Noe,* Vijayalakshmi Natarajan, Sheri L. Snow, Lilli A. Wolf-Gouveia, Peter G. Mitchell, Lori Lopresti-Morrow, Lisa M. Reeves, Sue A. Yocum, Ivan Otterness, Marcia A. Bliven, Thomas J. Carty, John T. Barberia, Francis J. Sweeney, Jennifer L. Liras and Marcie Vaughn



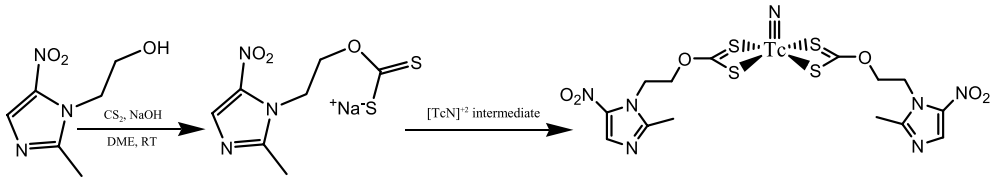
Deoxyribosyl analogues of methionyl and isoleucyl sulfamate adenylates as inhibitors of methionyl-tRNA and isoleucyl-tRNA synthetases pp 3389–3393
Sung Eun Kim, Su Yeon Kim, Sunghoon Kim, Taehee Kang and Jeewoo Lee*



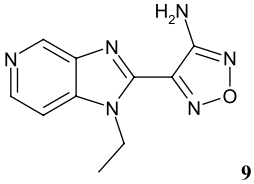
Synthesis of functionalized acetophenones as protein tyrosine phosphatase 1B inhibitors pp 3394–3397
Manish Dixit, Brajendra K. Tripathi, Arvind K. Srivastava and Atul Goel*



A novel [^{99m}Tc≡N]$^{2+}$ complex of metronidazole xanthate as a potential agent for targeting hypoxia pp 3398–3401
Madhava B. Mallia, Anupam Mathur, Suresh Subramanian, Sharmila Banerjee and H. D. Sarma, Meera Venkatesh*



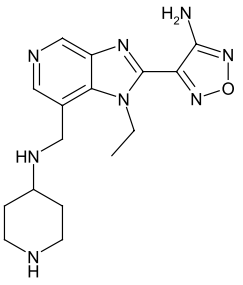
(1*H*-Imidazo[4,5-*c*]pyridin-2-yl)-1,2,5-oxadiazol-3-ylamine derivatives: A novel class of potent MSK-1-inhibitors pp 3402–3406
Mark J. Bamford,* Michael J. Alberti, Nicholas Bailey, Susannah Davies, David K. Dean, Alessandra Gaiba, Stephen Garland, John D. Harling, David K. Jung, Terence A. Panchal, Christopher A. Parr, Jon G. Steadman, Andrew K. Takle, James T. Townsend, David M. Wilson and Jason Witherington



9

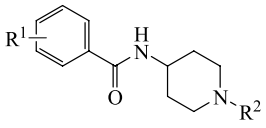
A novel series of imidazo[4,5-*c*]pyridines bearing a 1,2,5-oxadiazol-3-ylamine functionality has been developed. These are potent inhibitors of mitogen and stress-activated protein kinase-1 (MSK-1), and exemplified by the potent inhibitor **9**.

(1*H*-Imidazo[4,5-*c*]pyridin-2-yl)-1,2,5-oxadiazol-3-ylamine derivatives: Further optimisation as highly potent and selective MSK-1-inhibitors pp 3407–3411
Mark J. Bamford,* Nicholas Bailey, Susannah Davies, David K. Dean, Leann Francis, Terence A. Panchal, Christopher A. Parr, Sanjeet Sehmi, Jon G. Steadman, Andrew K. Takle, James T. Townsend and David M. Wilson



The novel imidazo[4,5-*c*]pyridine 1,2,5-oxadiazol-3-yl template affords an excellent start point for identification of inhibitors of a number of protein kinases. Here we report on its optimisation for mitogen and stress-activated protein kinase-1 (MSK-1) inhibitory activity, and selectivity over other kinases.

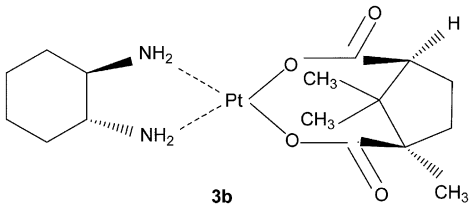
Identification of aminopiperidine benzamides as MCHr1 antagonists pp 3412–3416
Anil Vasudevan,* Mary K. Verzal, Derek Wodka, Andrew J. Souers, Christopher Blackburn, Jennifer Lee Che, Sujen Lai, Sevan Brodjian, Doug H. Falls, Brian D. Dayton, Elizabeth Govek, Tom Daniels, Brad Geddes, Kennan C. Marsh, Lisa E. Hernandez, Christine A. Collins and Philip R. Kym



The identification of a novel series of benzamide-containing MCHr1 antagonists is described.

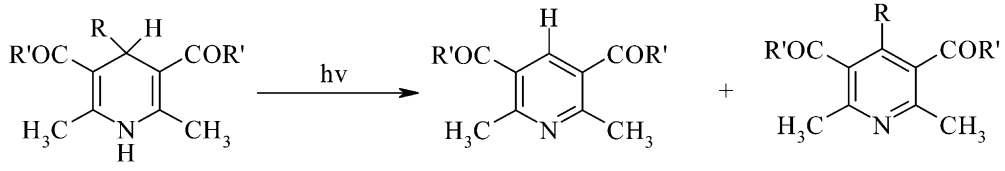
Potential new antitumor agents from an innovative combination of camphorato, a ramification of traditional Chinese medicine, with a platinum moiety pp 3417–3422
Lianhong Wang, Shaohua Gou,* Yongjiang Chen and Yun Liu

Eight new camphorato platinum complexes have been synthesized and evaluated for their in vitro cytotoxicity against four human tumor cell lines. The antitumor activities of compounds **3a** and **b** were assayed in vivo against LS-174T human colon carcinoma cell line. Complex **3b** exhibited not only higher in vivo antitumor activity, but also less toxicity than oxaliplatin when it was administered intravenously three times at a dose of 6mg/kg.



3b

Solid state photochemistry of 1,4-dihydropyridines pp 3423–3425
Hamid R. Memarian* and Arsalan Mirjafari



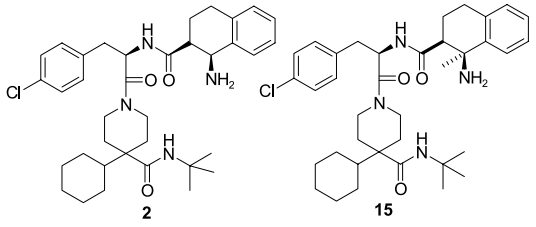
R':OCH_2CH_3 **1** **2** **3**

R':CH_3 **4** **5** **6**

4,4′-Dimethoxytrityl group derived from secondary alcohols: Are they removed slowly under acidic conditions? pp 3426–3429
R. Krishna Kumar and Vasulinga T. Ravikumar*

Removal of 4,4′-dimethoxytrityl (DMT) groups from primary and secondary hydroxyl functionality was investigated. It was observed that deblocking of DMT group from secondary hydroxyl group of molecules attached to solid support under acidic conditions occurred relatively slowly compared to primary hydroxyl group. Marginal difference in rate of detritylation was observed between DMT group attached to 5′-hydroxyl group of deoxyribonucleoside and 2′-*O*-methoxyethylribonucleoside when attached to one kind of support. Removal of DMT from nucleoside attached to OligoPrep solid support was found to be slow.

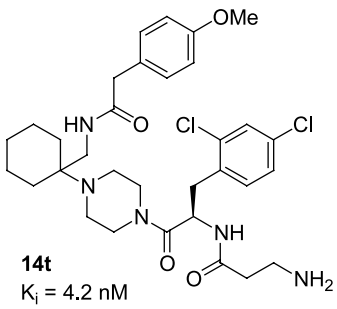
1-Amino-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid as a Tic mimetic: Application in the synthesis of potent human melanocortin-4 receptor selective agonists pp 3430–3433
Raman K. Bakshi,* Qingmei Hong, J.T. Olson, Zhixiong Ye, Iyassue K. Sebhat, David H. Weinberg, Tanya MacNeil, Rubana N. Kalyani, Rui Tang, William J. Martin, Alison Strack, Erin McGowan, Constantin Tamvakopoulos, Randy R. Miller, Ralph A. Stearns, Wei Tang, D. Euan Maclntyre, Lex H.T. van der Ploeg, Arthur A. Patchett and Ravi P. Nargund



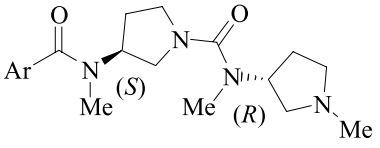
2 15

The discovery of 1-amino-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid analogs as potent human melanocortin-4 selective agonists is described.

Structure–activity relationship of a series of cyclohexylpiperidines bearing an amide side chain as antagonists of the human melanocortin-4 receptor **pp 3434–3438**
Joseph A. Tran, Joseph Pontillo, Melissa Arellano, Beth A. Fleck, Fabio C. Tucci, Dragan Marinkovic, Caroline W. Chen, John Saunders, Alan C. Foster and Chen Chen*

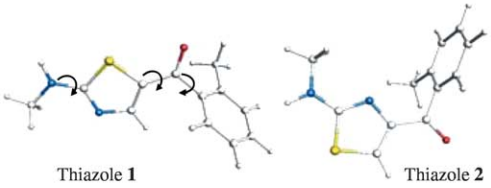


Synthesis and structure–activity relationships of biarylcarboxamide bis-aminopyrrolidine urea derived small-molecule antagonists of the melanin-concentrating hormone receptor-1 (MCH-R1) **pp 3439–3445**
Martin W. Rowbottom,* Troy D. Vickers, Brian Dyck, Junko Tamiya, Mingzhu Zhang, Liren Zhao, Jonathan Grey, David Provencal, David Schwarz, Christopher E. Heise, Monica Mistry, Andrew Fisher, Teresa Dong, Tao Hu, John Saunders and Val S. Goodfellow



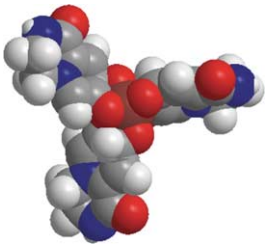
The design and synthesis of a number of bis-aminopyrrolidine ureas are described and the results from SAR studies are summarized. The best compounds showed K_i = 1 nM.

Isomeric thiazole derivatives as ligands for the neuropeptide Y5 receptor **pp 3446–3449**
Matthias Nettekoven,* Wolfgang Guba, Werner Neidhart, Patrizio Mattei, Philippe Pflieger, Olivier Roche and Sven Taylor



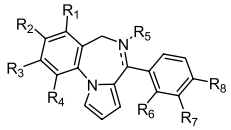
Sets of isomeric thiazole derivatives **1** and **2** were synthesised and compared with respect to their conformational energies.

Novel iron-specific fluorescent probes **pp 3450–3452**
Yongmin Ma, Wei Luo, Michel Camplo, Zudong Liu and Robert C. Hider*



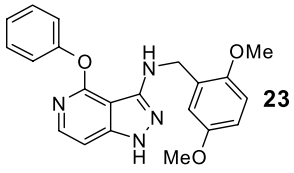
A series of novel iron-specific fluorescent probes is reported where the chelator function unusually forms part of the fluorescent moiety. The ability of this range of molecules to permeate human erythrocyte ghost membranes was investigated.

Pyrrolo[1,2-*a*][1,4]benzodiazepine: A novel class of non-azole anti-dermatophyte anti-fungal agents **pp 3453–3458**
Lieven Meerpoel,* Jef Van Gestel, Frans Van Gerven, Filip Woestenborghs, Patrick Marichal, Vic Sipido, Gilkerson Terence, Roger Nash, David Corens and Ray D. Richards



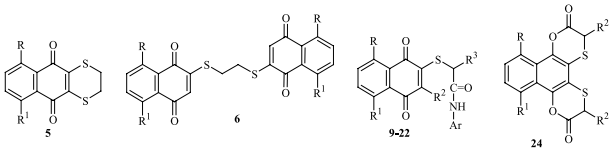
The anti-fungal structure–activity relationship of this novel class of 5,6-dihydro-4*H*-pyrrolo[1,2-*a*][1,4]benzodiazepines is described together with its mode of action that appeared to be the inhibition of squalene epoxidase.

Structure-driven HtL: Design and synthesis of novel aminoindazole inhibitors of c-Jun N-terminal kinase activity **pp 3459–3462**
Michael J. Stocks,* Simon Barber, Rhonan Ford, Frederic Leroux, Steve St-Gallay, Simon Teague and Yafeng Xue



The design and synthesis of a new series of c-Jun N-terminal kinase inhibitors are reported. Compound **23** displayed the greatest activity within the series.

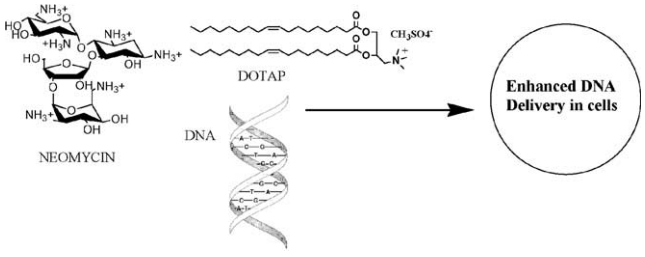
Synthesis and biological evaluation of novel 1,4-naphthoquinone derivatives as antibacterial and antiviral agents **pp 3463–3466**
Vishnu K. Tandon,* Dharmendra B. Yadav, Ravindra V. Singh, Meenu Vaish, Ashok K. Chaturvedi and Praveen K. Shukla



The synthesis, and antibacterial and antiviral activities of **5**–**24** are described.

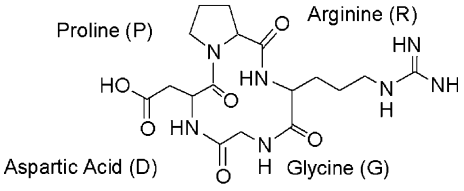
Neomycin improves cationic lipid-mediated transfection of DNA in human cells **pp 3467–3469**
Sara Napoli, Giuseppina M. Carbone, Carlo V. Catapano,* Nick Shaw* and Dev. P. Arya*

Delivery of oligonucleotides has been a major impediment in the development of nucleic acid based drugs. In this report, we show that neomycin, an aminoglycoside antibiotic, when combined with a cationic lipid preparation such as DOTAP, enhances transfection efficiency of both reporter plasmids and oligonucleotides and results in a significant increase in transgene expression. The results described here open a new lead in ongoing efforts for oligonucleotide delivery.



NEOMYCIN MEDIATED ENHANCED DNA DELIVERY

RGD mounted on an L-proline scaffold **pp 3470–3471**
Eric Enholm* and Ashwin Bharadwaj



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Instructions to contributors **pp III–VI**

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Ameliorating transthyretin amyloidogenesis by native state kinetic stabilization mediated by small molecule binding. Small molecule binding to the amyloidogenic protein transthyretin kinetically stabilizes the native tetrameric state, preventing dissociation to folded monomers that misfold and misassemble into toxic intermediates, amorphous aggregates, and amyloid fibrils. The Kelly laboratory has developed several structurally distinct inhibitor families, depicted in the background, that are undergoing pharmacological evaluation. Created by Steven M. Johnson, graduate student in Professor Jeffery W. Kelly's laboratory, Department of Chemistry, The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 N. Torrey Pines Road, La Jolla, CA 92037, USA.

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