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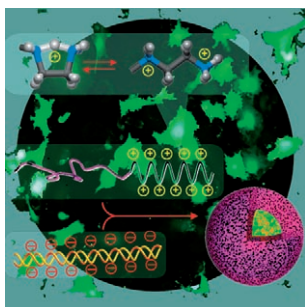
Full text:



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Some articles in this issue have already appeared online in Wiley InterScience. See www.chemmedchem.org under EarlyView®

COVER PICTURE



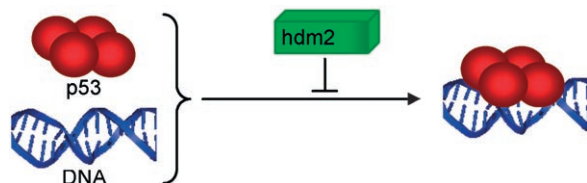
The cover picture shows highly transfection-efficient and less toxic polyplex micelles formed by the electrostatic interaction between DNA and block cationomers equipped with an ethylenediamine unit at the side chain. The cationomers undergo a conformational transition of the ethylenediamine unit from the *gauche* (mono-protonated) to the *anti* (di-protonated) form as the pH decreases from physiological to acidic conditions, providing a high buffering capacity for efficient transfection. The polyplex micelles showed effective and non-cytotoxic transfection of a green fluorescent protein (GFP) gene into mouse primary osteoblast cells (background). For more details, see the full paper by N. Kanayama et al. on p. 439 ff.

NEWS

From our sister journals

396 – 397

REVIEWS



Blocked at the interface: The discovery and design of small molecules that impede specific protein–protein interactions such as that between p53 and hdm2 represent a research field with

strong potential for the development of anticancer drugs. This field is faced with some unique challenges that are different from those faced by drug-discovery programs focused on enzyme inhibitors.

P. Chène*

400 – 411

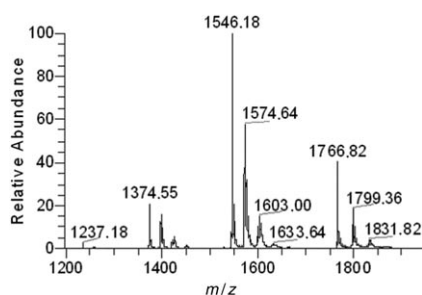
Drugs Targeting Protein–Protein Interactions

COMMUNICATIONS

A. Casini, C. Gabbiani, G. Mastrobuoni,
L. Messori,* G. Moneti, G. Pieraccini

413–417

Exploring Metallodrug–Protein Interactions by ESI Mass Spectrometry: The Reaction of Anticancer Platinum Drugs with Horse Heart Cytochrome c



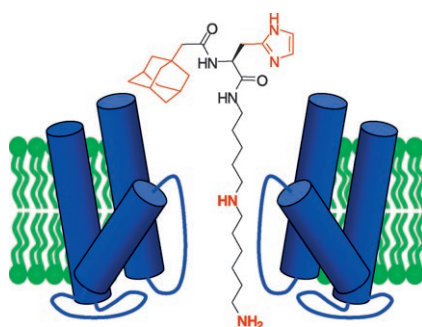
Under the right conditions, as shown by high-quality ESI-MS spectra, a variety of platinum–protein adducts are formed from the reaction of various platinum drugs with cytochrome c. Met65 is proposed as the primary site for platinum coordination. Direct comparative information was obtained on the reactivity of these classical anticancer platinum compounds with proteins, and the mechanistic and methodological implications of these findings are discussed.

FULL PAPERS

L. S. Jensen, U. Bølcho, J. Egebjerg,
K. Strømgaard*

419–428

Design, Synthesis, and Pharmacological Characterization of Polyamine Toxin Derivatives: Potent Ligands for the Pore-Forming Region of AMPA Receptors

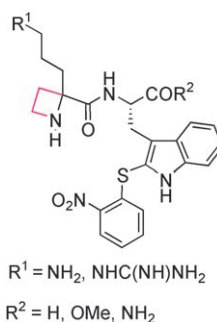


Spiders and wasps produce small-molecule toxins that are known to affect important receptors in the brain. A small library of derivatives of such structures was prepared, providing very potent and highly selective blockers of certain glutamate-gated ion channels, which are potential leads for the treatment of neurodegenerative diseases.

M. A. Bonache, C. García-Martínez,
L. García de Diego, C. Carreño,
M. J. Pérez de Vega, M. T. García-López,
A. Ferrer-Montiel,* R. González-Muñiz*

429–438

Old Molecules for New Receptors: Trp(Nps) Dipeptide Derivatives as Vanilloid TRPV1 Channel Blockers



Under restraint. The first experimental evidence for the vanilloid receptor as the possible molecular integrator of the central analgesic activity displayed by Trp(Nps)-containing dipeptides is provided. The incorporation of conformationally restricted azetidines-derived Arg (shown in pink), led to more selective derivatives than the reference linear compounds in some instances.

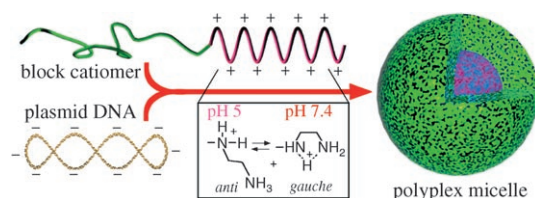
N. Kanayama, S. Fukushima,
N. Nishiyama,* K. Itaka, W.-D. Jang,
K. Miyata, Y. Yamasaki,
U.-i. Chung, K. Kataoka*

439–444

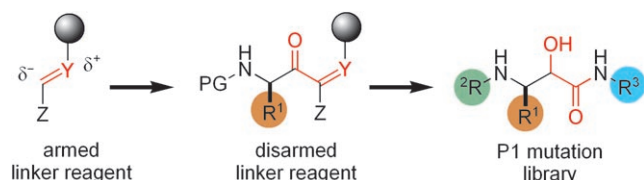
A PEG-Based Biocompatible Block Cationer with High Buffering Capacity for the Construction of Polyplex Micelles Showing Efficient Gene Transfer toward Primary Cells



A polymer that delivers! A poly(ethylene glycol)-based block cationer with an ethylenediamine unit as a side chain was prepared by an aminolysis reaction,



and its utility as a gene carrier was investigated. This polymer provided efficient and less toxic transfection even toward primary cells.



The use of phosphoranones as linker reagents in C-acylations allows the direct incorporation of peptide isosteres in solid-phase synthesis. This approach led to the discovery that the P1 site of pep-

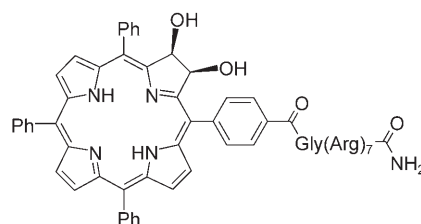
tidomimetic aspartic protease inhibitors can adopt an unpredicted binding mode. The results of this study will be valuable for increasing the affinity and selectivity of future protease inhibitors.

S. Weik, T. Luksch, A. Evers, J. Böttcher, C. A. Sotriffer, A. Hasilik, H.-G. Löffler, G. Klebe, J. Rademann*

445 – 457

The Potential of P1 Site Alterations in Peptidomimetic Protease Inhibitors as Suggested by Virtual Screening and Explored by the Use of C–C-Coupling Reagents

Good things come in sevens: A membrane-penetrating (arginine)₇ oligopeptide was used as a delivery vector for a chlorin-based photosensitizer (shown). The appended peptide dramatically increases the effectiveness of tumor cell death by photodynamic therapy through improved aqueous solubility and cellular uptake of the photosensitizer.

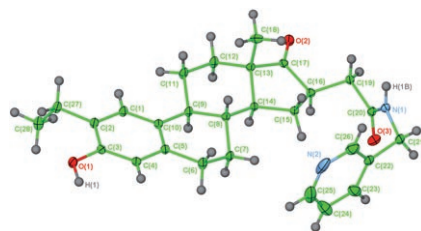


Y. Choi, J. R. McCarthy, R. Weissleder, C.-H. Tung*

458 – 463

Conjugation of a Photosensitizer to an Oligoarginine-Based Cell-Penetrating Peptide Increases the Efficacy of Photodynamic Therapy

Targeting breast cancer: The X-ray crystal structure confirms the β orientation at position 16 of the estrone template used in the synthesis of the molecule shown, which is a potent inhibitor of 17 β -HSD1 (IC_{50} = 27 nM) and is selective over 17 β -HSD2. Novel focused libraries of 16-substituted estrone derivatives and modified E-ring steroids as new 17 β -HSD1 inhibitors are described.



N. Vicker, H. R. Lawrence, G. M. Allan, C. Bubert, A. Smith, H. J. Tutill, A. Purohit, J. M. Day, M. F. Mahon, M. J. Reed, B. V. L. Potter*

464 – 481

Focused Libraries of 16-Substituted Estrone Derivatives and Modified E-Ring Steroids: Inhibitors of 17 β -Hydroxysteroid Dehydrogenase Type 1

A series of prenylflavonoids that belong to a group of nonsteroidal phytoestrogens act as potent estrogenic compounds. The molecular mechanisms of these compounds were explored with biological assays and computer-aided simulations. The interactions between these compounds and the estrogen receptor showed important structure–activity relationships in the initiation of estrogen-like activity.



Z.-q. Wang, N. Weber, Y.-j. Lou,* P. Proksch

482 – 488

Prenylflavonoids as Nonsteroidal Phytoestrogens and Related Structure–Activity Relationships

Supporting information on the WWW (see article for access details).

* Author to whom correspondence should be addressed.

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Issue 3, 2006, was published online on March 1, 2006.

ChemMedChem is indexed in *Chemical Abstracts Service/SciFinder*, *ChemInform*, *Chemistry Citation Index*, *COMPENDEX*, *EMBASE/Excerpta Medica*, *EMNursing*, *GEOBASE/Geographical & Geological Abstracts*, *Mosby Yearbooks*, and *SCOPUS*.

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