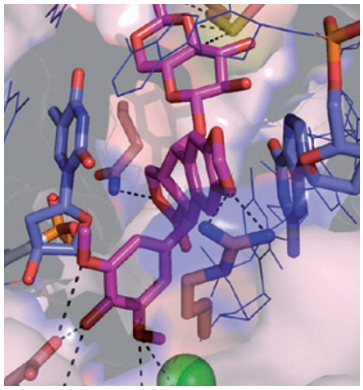
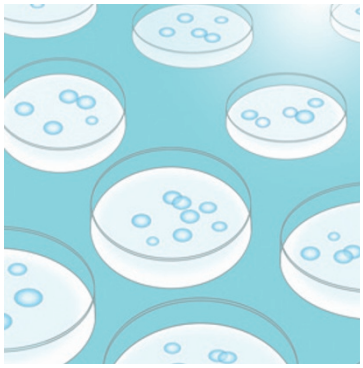
IN THIS ISSUE



Interfacial inhibition p25



Antimicrobial peptides p37

This month we are delighted to be celebrating 10 years of *Nature Reviews Drug Discovery* (see the editorial on page 3). Reflecting our continuing aim to feature articles across the broad spectrum of areas relevant to drug discovery and development, our Review articles this month cover an array of topics. The threat of antibiotic resistance necessitates the development of improved drugs, and Schneider and colleagues present an emerging strategy based on the exploitation of naturally occurring host defence antimicrobial peptides (AMPs). They discuss how recent advances in computer-assisted peptide design strategies are enabling the creation of more potent, broad-spectrum AMPs that may lead to next-generation antibiotics. Meanwhile, Pommier and Marchand discuss the concept of interfacial inhibition, an effective approach for targeting complex macromolecular systems, which involves the selective binding of an agent to the interface of macromolecules within a complex undergoing a conformational change. Exemplified by antibiotic, antiviral and anticancer agents, they define the mechanisms of action of interfacial inhibitors and discuss the implications for future drug discovery. Cancer is one of a range of diseases in which serine hydrolases — a large and diverse class of enzymes — are therapeutic targets. Bachovchin and Cravatt focus on the therapeutic potential of the mammalian serine hydrolases, many of which are poorly characterized and lack selective chemical inhibitors, and describe strategies for the discovery of novel inhibitors. Finally, Hollenberg and colleagues summarize the activation and signalling mechanisms of the G protein-coupled proteinase-activated receptors, and discuss their potential as therapeutic targets in cardiovascular, musculoskeletal, gastrointestinal, respiratory and central nervous system disorders.

EDITORIAL OFFICE

LONDON NatureReviews@nature.com
The Macmillan Building, 4 Crinan Street,
London N1 9XW, UK
Tel: +44 (0)20 7843 3620; Fax: +44 (0)20 7843 3629
E-mail: NatureReviews@nature.com

To subscribe and for more detailed information visit
www.nature.com/nrd

CHIEF EDITOR: Peter Kirkpatrick
SENIOR EDITORS: Alexandra Flemming, Charlotte Harrison, Sarah Crunkhorn, Monica Hoyos Flight
NEWS EDITOR: Asher Mullard
COPY EDITOR: Mariam Faruqi
SENIOR COPY EDITOR (NRD): Man Tsuey Tse
SENIOR COPY EDITORS: Yukie Ozawa, Catriona Rodwell, Lucie Wootton
COPY EDITING MANAGER: Lewis Packwood
ART CONTROLLER: Susanne Harris
SENIOR ART EDITORS: Vicky Summersby, Patrick Morgan, Kirsten Lee

MANAGING PRODUCTION EDITOR: Judith Shadwell
SENIOR PRODUCTION EDITOR: Simon Fenwick
PRODUCTION CONTROLLER: Natalie Smith
SENIOR EDITORIAL ASSISTANT: Laura Corns
EDITORIAL ASSISTANT: Ella Lines
WEB PRODUCTION MANAGER: Deborah Anthony
MARKETING MANAGERS: Tim Redding, Virginia Lee
PUBLISHING DIRECTOR: Peter Collins

NEW YORK nature@natureny.com
Nature Publishing Group, 75 Varick Street, 9th floor,
New York, NY 10013–1917, USA
Tel: +1 212 726 9200; Fax: +1 212 696 9006

PUBLISHER (BIOPHARMA): Melanie Brazil

CUSTOMER SERVICES Feedback@nature.com

Printed in Wales by Cambrian Printers on acid-free paper

EDITORS

PETER KIRKPATRICK

ALEXANDRA FLEMMING

CHARLOTTE HARRISON

SARAH CRUNKHORN

MONICA HOYOS FLIGHT

ASHER MULLARD