



nature publishing group



► **COVER:** 'Alternative signalling pathways' by Susanne Harris, inspired by the Review on p373.



PETER KIRKPATRICK



ALEXANDRA FLEMING



CHARLOTTE HARRISON



SARAH CRUNKHORN



BETHAN HUGHES



MONICA HOYOS FLIGHT

Traditionally, signalling through seven-transmembrane receptors (7TMRs) — which are one of the largest classes of drug targets — was thought to be mediated solely via G proteins. Recently, however, it has been increasingly appreciated that β -arrestins, which mediate receptor desensitization, can also initiate their own functionally distinct signalling pathways. In the first review this month, Lefkowitz and colleagues describe recent advances in the characterization of β -arrestin-mediated signalling at 7TMRs, and consider the implications for drug discovery. Another review also highlights the therapeutic significance of emerging knowledge of cell signalling pathways: those mediated through the activation of store-operated calcium release-activated calcium (CRAC) channels. Parekh summarizes the gating and function of CRAC channels, and considers both their potential as therapeutic targets — in particular, in immuno-inflammatory diseases — and the development of channel blockers. Both perspective articles this month discuss approaches that may contribute to reducing attrition rates in drug development. Genomic knowledge is revealing potential biomarkers in oncology that could be used to improve success in clinical trials by targeting treatments to patients who are more likely to respond. In the first article, Schilsky focuses on the opportunities and challenges in developing anticancer drugs in biomarker-defined populations, emphasizing the need for more personalized therapy. Second, Ebert and Svendsen discuss the potential of using embryonic or induced pluripotent stem cells to improve drug screening, and also to model diseases such as neurodegenerative disorders. Finally, Citron reviews the development of disease-modifying therapies for the most common neurodegenerative disorder, Alzheimer's disease, highlighting approaches, such as those that target amyloid- β , for which clinical data could soon clarify their true potential.

EDITORIAL OFFICESLONDON NatureReviews@nature.comThe Macmillan Building,
4 Crinan Street,London N1 9XW, UK
Tel: +44 (0)20 7843 3620;

Fax: +44 (0)20 7843 3629

CHIEF EDITOR: Peter Kirkpatrick**SENIOR EDITORS:** Alexandra Fleming,
Charlotte Harrison, Sarah Crunkhorn**ASSOCIATE EDITOR:** Monica Hoyos Flight**SENIOR NEWS EDITOR:** Bethan Hughes**ASSISTANT EDITORS:** Man Tsuey Tse,
Katie Kingwell**COPY EDITOR:** Kate Hedigan**ART CONTROLLER:** Susanne Harris**SENIOR ART EDITORS:** Vicky Summersby,
Patrick Morgan**MANAGING PRODUCTION EDITOR:**

Judith Shadwell

SENIOR PRODUCTION EDITOR: Simon Fenwick**PRODUCTION CONTROLLER:** Natalie Smith**EDITORIAL ASSISTANTS:** Jacques Smit,

Laura Corns

WEB PRODUCTION MANAGER:

Deborah Anthony

MARKETING MANAGERS: Tim Redding,
Samantha Savallo**MANAGEMENT OFFICES**LONDON nature@nature.comThe Macmillan Building, 4 Crinan Street,
London N1 9XW, UK

Tel: +44 (0)20 7833 4000;

Fax: +44 (0)20 7843 4596/7

OFFICE MANAGER: Laura Firman**PUBLISHING DIRECTOR:** Peter Collins**MANAGING DIRECTOR:**

Steven Inchcoombe

EDITOR-IN-CHIEF, NATURE PUBLICATIONS:

Philip Campbell

ASSOCIATE DIRECTORS: Jenny Henderson,
Tony Rudland**EDITORIAL PRODUCTION DIRECTOR:**

James McQuat

PRODUCTION DIRECTOR:

Yvonne Strong

DIRECTOR, WEB PUBLISHING: Dan Pollock**HEAD OF WEB PRODUCTION:**

Alexander Thurrell

NEW YORK nature@natureny.comNature Publishing Group,
75 Varick Street, 9th floor, New York,
NY 10013-1917, USA

Tel: +1 212 726 9200;

Fax: +1 212 696 9006

CHIEF (BIOPHARMA): Melanie Brazil**CHIEF TECHNOLOGY OFFICER:**

Howard Ratner

HEAD OF INTERNAL SYSTEMS DEVELOPMENT:

Anthony Barrera

HEAD OF SOFTWARE SERVICES:

Luigi Squillante

GLOBAL HEAD OF ADVERTISING AND**SPONSORSHIP:** Dean Sanderson**HEAD OF NATURE RESEARCH & REVIEWS****MARKETING:** Sara Girard**TOKYO** nature@natureasia.comChiyoda Building 5F, 2-37-1 Ichigayatamachi,
Shinjuku-ku, Tokyo 162-0843, Japan
Tel: +81 3 3267 8751; Fax: +81 3 3267 8746**ASIA-PACIFIC PUBLISHER:** Antoine E Bocquet**MANAGER:** Koichi Nakamura**ASIA-PACIFIC SALES DIRECTOR:**

Kate Yoneyama

SENIOR MARKETING MANAGER:

Peter Yoshihara

MARKETING/PRODUCTION MANAGER:

Takesh Murakami

INDIA 5A/12 Ansari Road, Daryaganj,

New Delhi 110 002, India

Tel/Fax: +91 11 2324 4186

SALES AND MARKETING MANAGER, INDIA:

Harpal Singh Gill

Copyright © 2010 Nature Publishing Group

Research Highlight images courtesy of

Getty Images unless otherwise credited.

Printed in Wales by Cambrian Printers on

acid-free paper