

Targeting interleukin-6 p395

# CONTENTS

June 2018  
Volume 17 no. 6

## REVIEWS

### 395 Interleukin-6: designing specific therapeutics for a complex cytokine

*Christoph Garbers, Sylvia Heink, Thomas Korn and Stefan Rose-John*

Dysregulation of IL-6 signalling is associated with inflammatory and lymphoproliferative disorders, and several classes of therapeutics have been developed that target components of the IL-6 signalling pathway. This Review describes the progress made in recent years in inhibiting IL-6-signalling and analyses the advantages and disadvantages of these approaches.

### 413 Post-exposure treatments for Ebola and Marburg virus infections

*Robert W. Cross, Chad E. Mire, Heinz Feldmann and Thomas W. Geisbert*

Efforts towards developing post-exposure therapies for infections with filoviruses, particularly Ebola and Marburg viruses, increased substantially during the Ebola virus outbreak of 2013–2016. Geisbert and colleagues review the progress made on this front and discuss the challenges and opportunities for developing post-exposure therapies in the future.

### 435 RNA-modifying proteins as anticancer drug targets

*P. Ann Boriack-Sjodin, Scott Ribich and Robert A. Copeland*

Covalent modifications of RNA — mediated by RNA-modifying proteins (RMPs) — affect RNA stability and translation to proteins, and some of these RMPs have been implicated in cancer. Here, Copeland and colleagues review the current understanding of RNA modifications with a focus on mRNA methylation and assess the potential of RMPs as novel anticancer targets.

## ADVERTISEMENT FEATURE

### BIOPHARMA DEALMAKERS

In this edition, the features analyse the commercial landscape for infectious disease R&D, how to develop IP strategies and deals in the fibrosis field. The features follow the Review that finishes on p453 and were produced thanks to the commercial support of the organizations featured in the advertorial profiles.

Nature Reviews Drug Discovery (ISSN 1474-1776) is published monthly by Nature America, Inc. p, 1 New York Plaza STE 4500, New York NY 10004-1562, USA. US Periodicals postage paid at New York, NY and additional mailing post offices. US POSTMASTER: Send address changes to Nature America, Inc., Subscription Dept, 1 New York Plaza STE 4500, New York NY 10004-1562, USA.

Copyright © 2018 Macmillan Publishers Limited, part of Springer Nature. All rights reserved. Printed in USA. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic or otherwise) without prior permission from [permissions@nature.com](mailto:permissions@nature.com).

## [www.nature.com/nrd](http://www.nature.com/nrd)

**POWERPOINT SLIDES** Figures and tables can be downloaded as PowerPoint files for use in presentations and for teaching.

**E-ALERT SIGN-UP** Get FREE monthly e-mail alerts to the content of this journal by registering online. Or sign up to receive the latest content as an RSS newsfeed by visiting [www.nature.com/nrd](http://www.nature.com/nrd)

**TWITTER** Follow *Nature Reviews Drug Discovery* on Twitter for the latest news from the journal and beyond: @NatRevDrugDisc

**ONLINE CORRESPONDENCE** Comments from readers about our articles. All correspondence will be highlighted on the table of contents and on e-mail alerts.

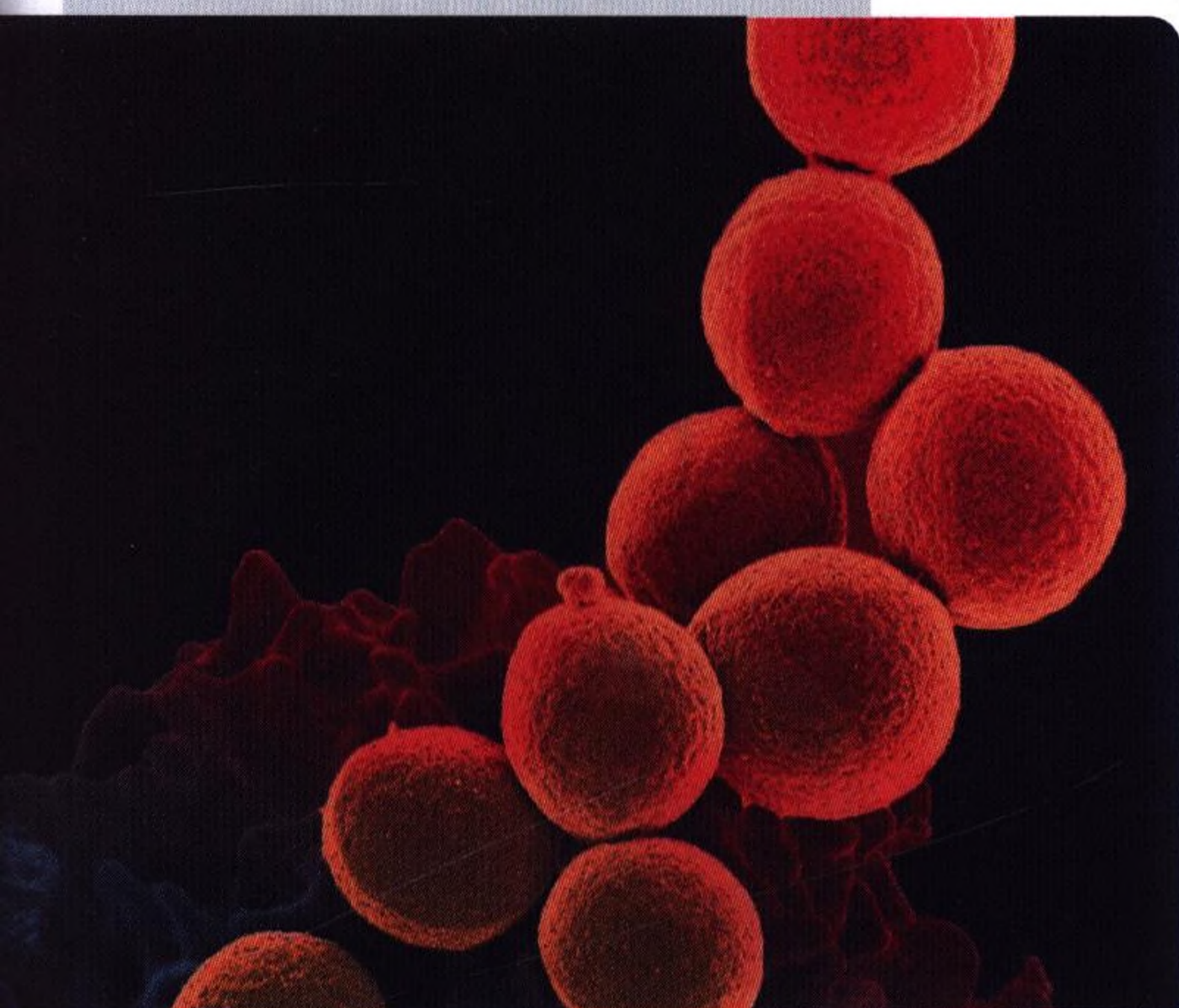
**COMPETING INTERESTS POLICY** Authors of articles in *Nature Reviews Drug Discovery* are required to declare any competing interests. For details, please see [www.nature.com/authors/policies/competing.html](http://www.nature.com/authors/policies/competing.html)

**ADVANCE ONLINE PUBLICATION** We operate an advance online publication (AOP) service for authors and readers to view the latest articles published online ahead of print.

**2-YEAR IMPACT FACTOR 57.000**

**2-YEAR MEDIAN 38**

For more information on journal metrics, please see [www.nature.com/ngp\\_/company\\_info/journal\\_metrics.html](http://www.nature.com/ngp_/company_info/journal_metrics.html)



Immunotherapeutic strategies for sepsis p381

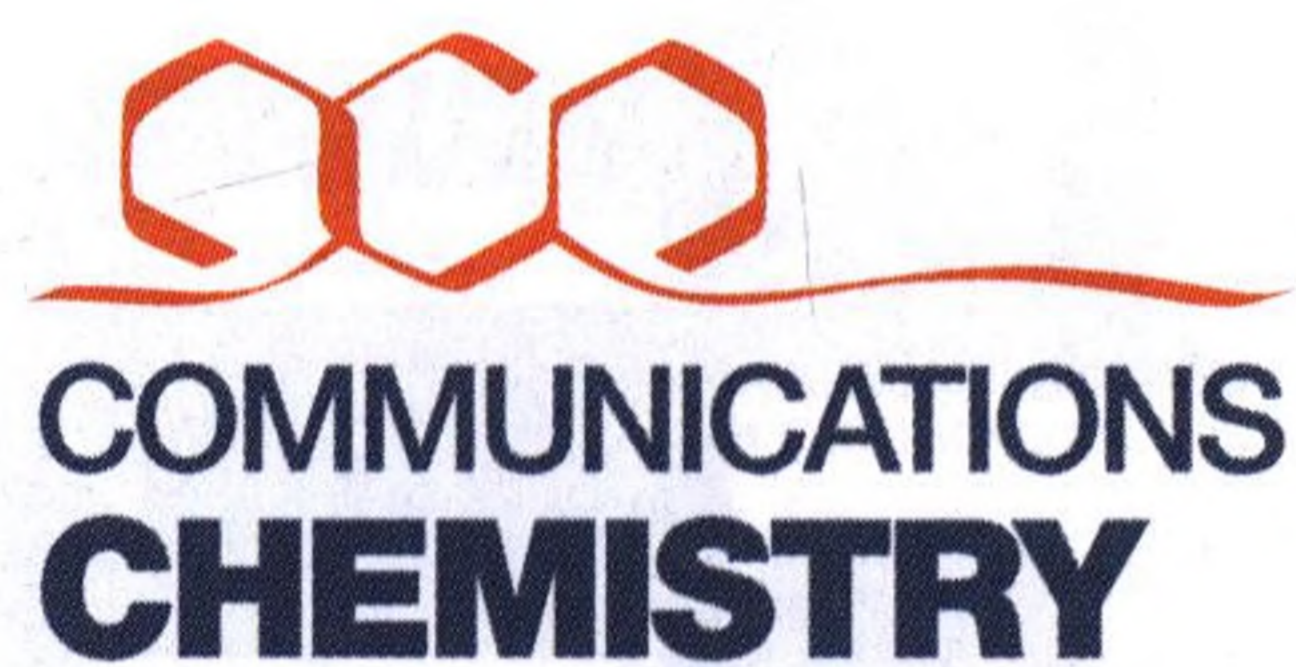
## COMMENT

- 379 **Accelerated approval of medicines: fit for purpose?**  
Alasdair Breckenridge and Lawrence Liberti

## NEWS &amp; ANALYSIS

## NEWS

- 381 **Sepsis researchers set sights on immunotherapeutic strategies**  
Two immune-boosting strategies have independently indicated promise in sepsis clinical trials, after years of failures with anti-inflammatories in this same space. Will it be enough to take sepsis drug development out of 'critical condition'?
- 383 **When drugs unintentionally affect gut bugs**  
Many drugs unexpectedly influence the human gut microbiome, showed a recent study, prompting questions about toxicity assays, clinical implications and repurposing opportunities.
- 385 **News in brief**  
BACE failures lower AD expectations, again | On the origin of transformative drugs | FDA approves first-in-class SYK inhibitor



## NOW PUBLISHING CONTENT

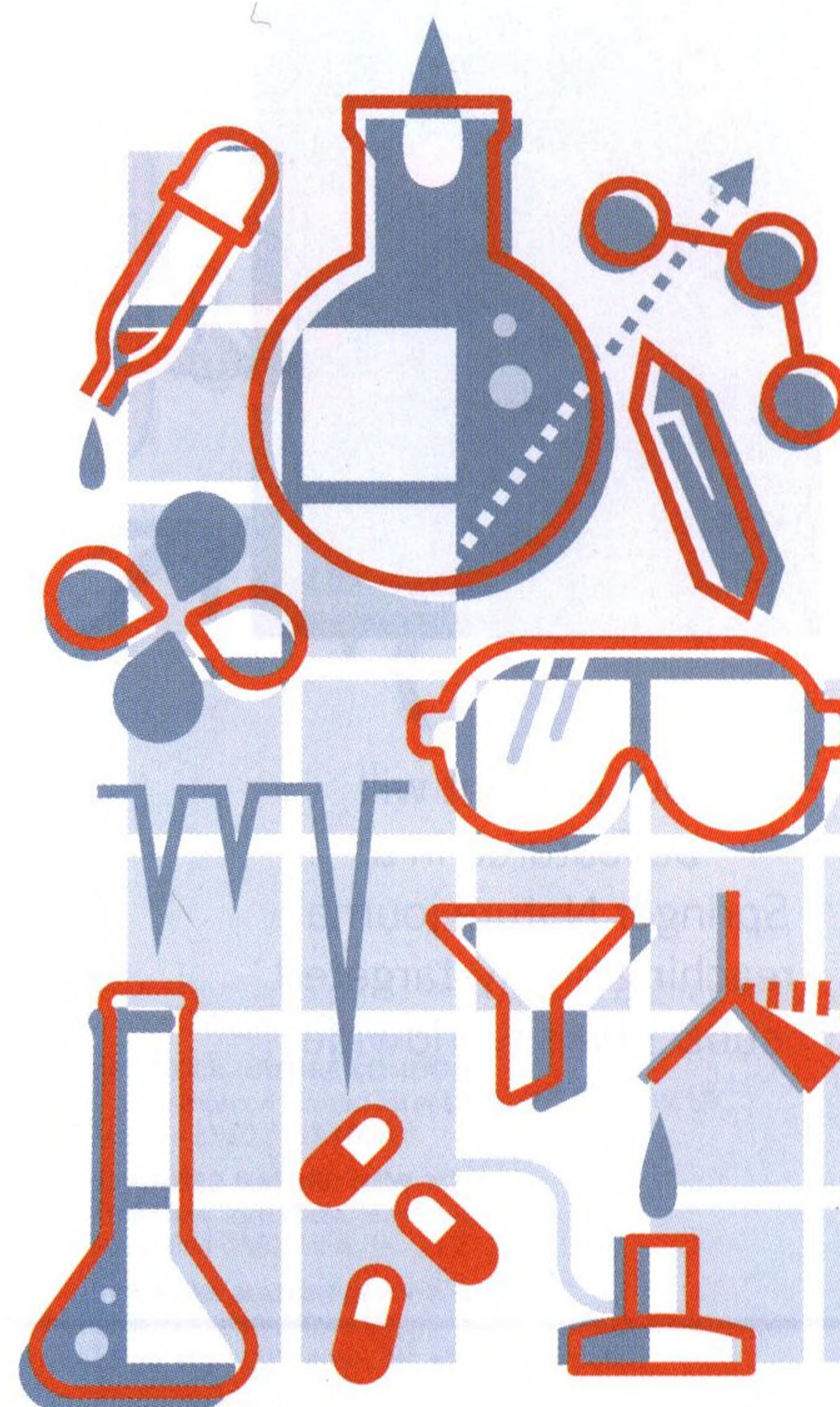
### A new open access journal for the chemical sciences from Nature Research

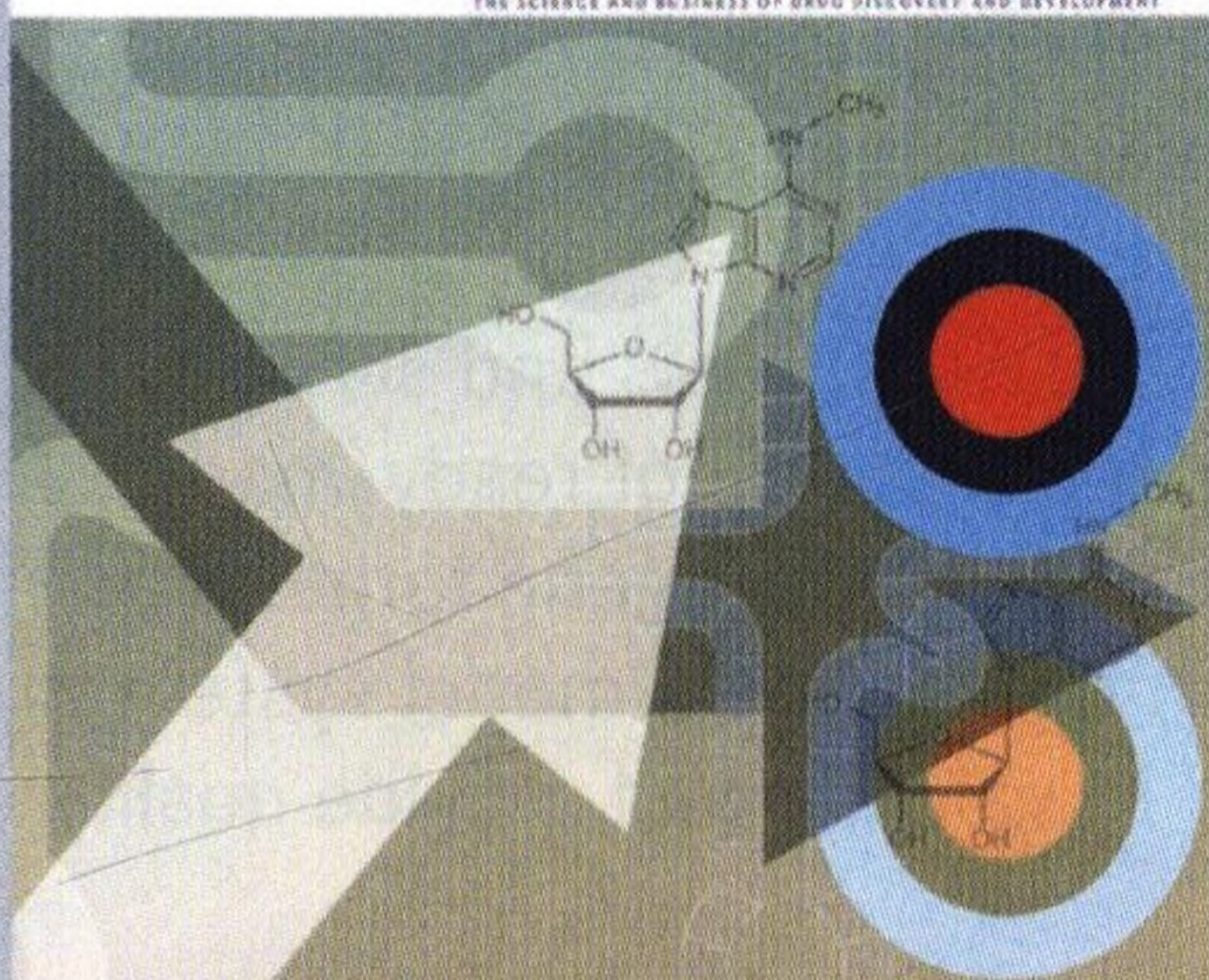
*Communications Chemistry* publishes high-quality primary research articles, reviews and commentary in all areas of the chemical sciences. Papers published in the journal represent significant advances that bring new insight to a specialized area of research.

All papers are handled by experienced in-house professional editors supported by an expert Editorial board.

#### Submit your research today and benefit from:

- Thorough peer review
- Fast decision process
- High Nature editorial standards
- High visibility
- CC-BY open access as standard





CANCER  
RNA-modifying proteins as drug targets

Interleukin-6  
Designing specific therapeutics for a complex cytokine

► COVER: 'RNA-modifying proteins as drug targets' by Susanne Harris, inspired by the Review on p435.

MEET THE EDITORS



PETER KIRKPATRICK



SARAH CRUNKHORN



MEGAN CULLY



M. TERESA VILLANUEVA



KATIE KINGWELL

EDITORIAL & PRODUCTION OFFICE

The Campus, 4 Crinan Street, London N1 9XW, UK  
Tel: +44 (0)20 7833 4000 | Email: nrdd@nature.com  
www.nature.com/nrd

CHIEF EDITOR Peter Kirkpatrick  
SENIOR EDITORS Sarah Crunkhorn, Megan Cully, M. Teresa Villanueva  
ASSOCIATE EDITOR (NEWS) Katie Kingwell  
COPY EDITOR Stephanie Wills  
SENIOR ART EDITOR Susanne Harris  
PRODUCTION EDITOR Melanie Gardeur  
JOURNAL ASSISTANTS Owen Stretton, Sivanjaa Manoj  
SENIOR EDITORIAL ASSISTANT Ashleigh Carver

CROSS-JOURNAL EDITORS Katharine Wrighton (Team Leader), Caroline Barranco and Isobel Leake (Seniors), Conor Bradley, Grant Otto and Shimona Starling (Associates)  
PROOFREADING SUPERVISOR Carrie Hardy

EDITORIAL ADMINISTRATION MANAGER Rebecca Cromie  
MANAGING PRODUCTION EDITOR Emma Carter  
SENIOR PRODUCTION EDITOR Simon Fenwick  
ASSISTANT PRODUCTION EDITOR Kate Snowdon  
PRODUCTION CONTROLLER Natalie Smith  
OFFICE AND ADMINISTRATION MANAGER Laura Lee  
EXECUTIVE EDITOR Arianne Heinrichs  
NATURE EDITORIAL DIRECTOR Ritu Dhand  
EDITORIAL DIRECTOR Alison Mitchell  
CUSTOMER SERVICES www.nature.com/help  
PERSONAL SUBSCRIPTIONS subscriptions@nature.com  
REPRINTS www.nature.com/reprints  
ADVERTISING & SPONSORSHIP www.nature.com/advertising  
SITE LICENCES www.nature.com/libraries/site\_licenses/index.html  
PRESS OFFICE press@nature.com  
MARKETING marketing@nature.com

MANAGEMENT OFFICES

SPRINGER NATURE LONDON  
The Campus, 4 Crinan Street, London, N1 9XW, UK.  
Tel: +44 (0)20 7833 4000

SPRINGER NATURE NEW YORK  
One New York Plaza, Suite 4500, New York, NY 10004-1562, USA. Tel: +1 212 726 9200

SPRINGER NATURE ASIA-PACIFIC  
Shiroyama Trust Tower 5F, 4-3-1 Toranomon, Minato-Ku, Tokyo 105-6005 Japan. Tel: +81 3 4533 8050

A list of other offices can be found at [www.nature.com/npg/\\_contact/offices.html](http://www.nature.com/npg/_contact/offices.html)

NEWS & ANALYSIS

AN AUDIENCE WITH...

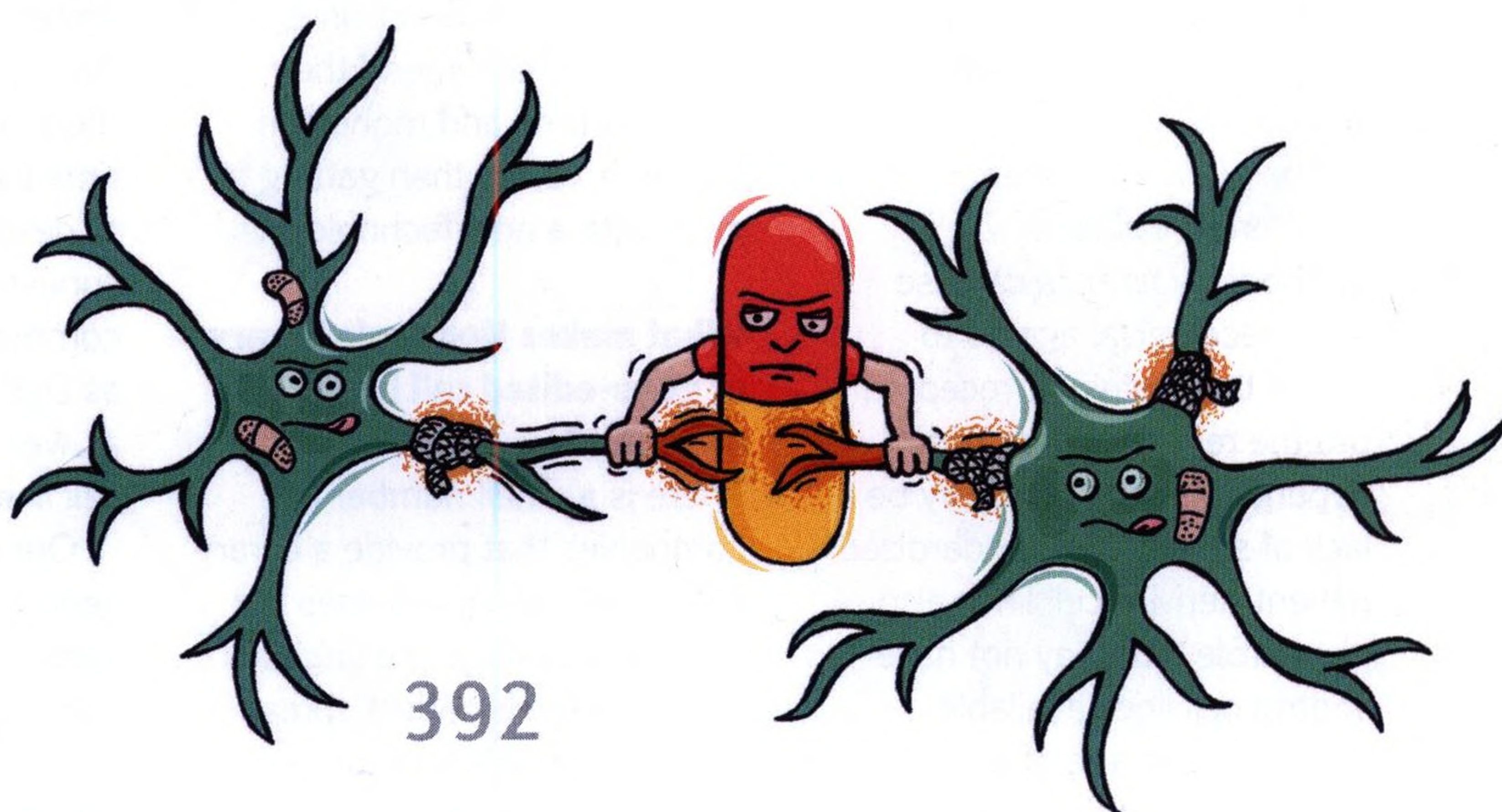
386 **Norbert Bischofberger**  
Norbert Bischofberger, former CSO of Gilead, discusses antiviral opportunities, Gilead's pivot to oncology and the need for a societal discussion of drug costs.

FROM THE ANALYST'S COUCH

389 **What drives site performance in clinical trials?**  
This article highlights results from a comprehensive study of the performance of clinical trial sites, which could help companies understand the underlying drivers of success.

RESEARCH HIGHLIGHTS

- 391 NEURODEGENERATIVE DISORDERS Rescuing mitochondrial motility
- 392 NEUROSCIENCE Reconnecting the brain after injury
- 393 CANCER Personalized cancer vaccines hit the spot
- 394 IN BRIEF Cancer | Autoimmune disease | Liver disease | Cancer ANTIBACTERIAL DRUGS Disrupting MRSA 'persisters'



392