IN THIS ISSUE

he dramatic failure of the cholesteryl ester transfer protein

inhibitor torcetrapib, designed to raise levels of high-density

lipoprotein (HDL) as a treatment for cardiovascular disease, in 2006 raised the question of whether raising HDL is a futile

strategy for atheroprotection. This month, Joy and Hegele review the complexity of the HDL system, discuss torcetrapib clinical trial data, and evaluate alternative strategies for HDL-based therapies. Meanwhile, in this month's perspective. Jia and colleagues suggest that humans can be viewed as "superorganisms with an indispensable internal ecosystem" — the gut microbiota. The authors propose that systems-oriented technologies such as metabonomics will shed light on complex host-bacteria interactions,

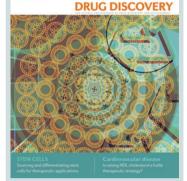
providing novel targets and therapeutic strategies to manipulate gut

potential as anti-obesity, anticancer and anti-infective drugs. Finally,

Klimanskaya and colleagues investigate two key factors that are crucial to the success of stem-cell-based therapies: the ability to find reliable sources of multipotent and pluripotent cells, and to control their differentiation.

microbiota associated with disease. The nature of the relationship between humans and members of their microbiome is also illustrated by the recent elucidation of the role of commensal bacteria in a physiological pathway that converts inorganic nitrate to nitric oxide (NO). In their Review, Lundberg and colleagues explore the significance of this alternative source of NO, and the possibility of targeting the nitrate-nitrite-NO pathway to treat a diverse range of diseases including myocardial infarction and stroke. Another simple physiological reaction, the conversion of carbon dioxide to bicarbonate ions and protons catalyzed by carbonic anhydrases (CAs), is also emerging as a target for a multitude of diseases. CA inhibitors were originally developed as diuretics and antiglaucoma drugs, but Supuran now discusses their emerging

nature REVIEWS



COVER: 'Stem cell differentiation' by Susanne Harris, inspired by the Review on p131.











EDITORIAL OFFICES

London N1 9XW, UK

Elinor Faulkner

Patrick Morgan

Judith Shadwell

Simon Fenwick

Tel: +44 (0)20 7843 3620;

Fax: +44 (0)20 7843 3629

CHIEF EDITOR: Peter Kirkpatrick

NEWS EDITOR: Bethan Hughes

COPY EDITOR: Man Tsuey Tse

Charlotte Harrison, Sarah Crunkhorn

ART CONTROLLER: Susanne Harris

EDITORIAL SUPPORT MANAGER:

SENIOR ART EDITORS: Vicky Askew,

MANAGING PRODUCTION EDITOR:

PRODUCTION CONTROLLER: Natalie Smith

DEPUTY PRODUCTION EDITOR:

LONDON NatureReviews@nature.com

The Macmillan Building, 4 Crinan Street,

ASSOCIATE EDITORS: Alexandra Flemming,

ASSISTANT EDITOR: Monica Hoyos Flight

EDITORIAL ASSISTANTS: Laura Firman. Robert Monk WEB PRODUCTION MANAGER, UK: Alexander Thurrell MARKETING MANAGERS: Kellie Lane, Leah Rodriguez MANAGEMENT OFFICES

LONDON nature@nature.com

The Macmillan Building, 4 Crinan Street, London N1 9XW, UK Tel: +44 (0)20 7833 4000-Fax: +44 (0)20 7843 4596/7 OFFICE MANAGER: Sheryl Ocampo PUBLISHING DIRECTOR: Peter Collins MANAGING DIRECTOR: Steven Inchcoombe EDITOR-IN-CHIEF, NATURE PUBLICATIONS: Philip Campbell ASSOCIATE DIRECTORS: Jenny Henderson, Tony Rudland EDITORIAL PRODUCTION DIRECTOR: lames McOuat

PRODUCTION DIRECTOR: Yvonne Strong DIRECTOR, WEB PUBLISHING: Timo Hanna HEAD OF WEB PRODUCTION: Jeremy Macdonald

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 CHIEF TECHNOLOGY OFFICER: Howard Ratin DIRECTOR OF NEW TECHNOLOGY: Greg Suprock HEAD OF WEB SERVICES: Anthony Barrera HEAD OF NATURE RESEARCH & REVIEWS MARKETING: Sara Girard

TOKYO nature@natureasia.com Chiyoda Building 5F, 2-37-1 Ichigayatamachi, Shinjuku-ku, Tokyo 162-0843, Japar 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 Yoshiha MARKETING/PRODUCTION MANAGER: Takesh Murakar

INDIA 5A/12 Ansari Road, Daryganj, New Delhi 110 002, India Tel/Fax: +91 11 2324 4186 SALES AND MARKETING MANAGER, INDIA: Harpal Singh Gill Copyright © 2008 Nature Publishing Group

Research Highlight images courtesy o Getty Images unless otherwise credited. Printed in Wales by Cambrian Printers on acid-free paper