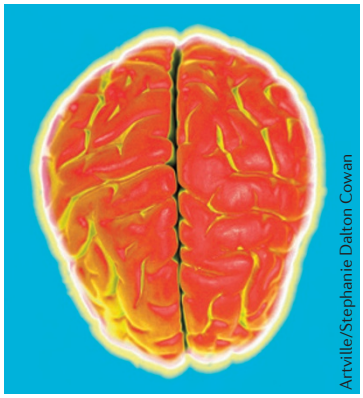
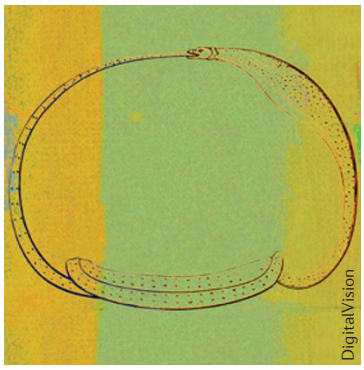
IN THIS ISSUE



Obesity and the brain p675



Targeting autophagy p709

Although the development of obesity drugs has been plagued by failure, two novel therapies have recently received US Food and Drug Administration approval, the first in 13 years. In their Review, Dietrich and Horvath consider the mechanisms of action of anti-obesity agents, including those currently in use, those withdrawn from the market and new compounds under development. They discuss the role of the hypothalamus in the control of food intake, proposing that agents designed to promote satiety are destined to fail owing to side effects, and suggest how approaches that aim to promote pathways involved in negative energy balance, such as those activated during exercise and calorie restriction, may be more likely to succeed. Leptin, a hormone that is produced by adipose tissue, acts on receptors in the hypothalamus to regulate appetite, body weight and glycaemia. However, although a potentially attractive candidate for the treatment of diabetes and obesity, clinical trials of leptin therapy have been disappointing, largely due to the existence of leptin resistance. Coppari and Bjørbæk review the roles of leptin and our current understanding of the cellular and molecular mechanisms mediating resistance to this hormone. They anticipate that a deeper understanding of this issue will enable the successful development of leptin-based therapeutics. An alternative strategy for treating diabetes and obesity may be the inhibition of autophagy. In fact, dysregulated autophagy has now been implicated in the pathology of a variety of disorders, including metabolic conditions, neurodegenerative diseases, cancers and infectious diseases. Rubinzstein and colleagues review the mechanisms of autophagy and the role of this pathway in different diseases, as well as strategies for therapeutic modulation.

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

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

CHIEF EDITOR: Peter Kirkpatrick
SENIOR EDITORS: Alexandra Flemming, Charlotte Harrison, Sarah Crunkhorn, Monica Hoyos Flight
SENIOR NEWS EDITOR: Asher Mullard
ASSISTANT EDITOR: Man Tsuey Tse
COPY EDITOR: Mariam Faruqi
SENIOR COPY EDITORS: Catriona Rodwell, Lucie Wootton, Isabel Woodman
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: Dipti Shah
MARKETING MANAGERS: Tim Redding, Nazly De La Rosa
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


ASHER MULLARD


MAN TSUEY TSE