nature in Sight FRONTIERS IN BIOLOGY

21 January 2016 / Vol 529 / Issue No 7586



Cover illustration 'Cryptic' by Nik Spencer

Editor, Nature Philip Campbell

Publishing Richard Hughes

Insights Editor Ursula Weiss

Production Editor Elizabeth Batty

Art Editor Nik Spencer

Sponsorship Reya Silao

Production lan Pope

Marketing Steven Hurst

Editorial Assistant Rebecca White

The Macmillan Building 4 Crinan Street London N1 9XW, UK Tel: +44 (0) 20 7833 4000 e: nature@nature.com



nature publishing group

The *Nature* Insight 'Frontiers in biology' aims to cover timely and important developments in biology, ranging from the subcellular to the organismal level, and including molecular mechanisms and biomedicine.

The collection begins with a Review on metastasis, which remains a significant challenge in the treatment of cancer. Metastases in some organs are less responsive to therapy than those in others. Joan Massagué and Anna Obenauf discuss the processes that underlie the colonization of various organs by cancer cells that escape from the primary tumour and enter the circulatory system. Improved understanding of these processes could facilitate the early diagnosis of metastases and lead to new therapeutic interventions.

Next, Michael Karin and Hans Clevers explore the cellular and molecular mechanisms of protective inflammation in tissue repair and regeneration, with a focus on the intestines and the liver. The positive effects of inflammation play an essential part in the restoration of tissue homeostasis, and offer protection from chronic inflammation, fibrosis and cancer.

Endothelial cells form the lining of blood vessels, but they also function in the development, growth and regeneration of organs through their release of paracrine signals known as angiocrine factors. Shahin Rafii and colleagues examine the emerging role of endothelial cells as signalling centres that orchestrate organ regeneration, morphogenesis and homeostasis.

Cells counteract endoplasmic reticulum stress — the abnormal accumulation of misfolded and unfolded proteins of the secretory pathway — by activating a homeostatic process called the unfolded protein response. Miao Wang and Randal Kaufman summarize our current understanding of this field at the molecular and cellular levels, as well as in relation to disease.

Resistance to antibiotics poses one of the most pressing threats to modern health care. Eric Brown and Gerard Wright consider the history and use of antibiotics, the factors that have led to the alarming rise in resistant pathogens, and the prospects for overcoming hurdles that hold back antibiotic discovery in the twenty-first century.

Barbara Marte, Sadaf Shadan, Clare Thomas, Christina Tobin Kåhrström & Ursula Weiss Senior Editors

CONTENTS

REVIEWS

298 Metastatic colonization by circulating tumour cells Joan Massagué & Anna C. Obenauf



- 307 Reparative inflammation takes charge of tissue regeneration Michael Karin & Hans Clevers
- **316 Angiocrine functions of organ-specific endothelial cells** *Shahin Rafii, Jason M. Butler & Bi-Sen Ding*



326 Protein misfolding in the endoplasmic reticulum as a conduit to human disease

Miao Wang & Randal J. Kaufman



336 Antibacterial drug discovery in the resistance era Eric D. Brown & Gerard D. Wright