A solitary figure walks through a somber urban landscape. The permeating tone of sadness in this painting gives an impression of life with major depressive disorder, whereas the light punctuating the scene hints at hope. Because depression has become a serious problem in societies around the world, it is crucial to investigate the basic mechanisms underlying this disease and to develop effective prevention and therapies. See the special section beginning on page 67. For the story behind the cover, go to http://scim.ag/cov6103.

REVIEW

60  Theory and Simulation in Neuroscience
W. Gerstner et al.
>> Depression section p. 67

REPORTS

84  The Shortest-Known-Period Star Orbiting Our Galaxy’s Supermassive Black Hole
L. Meyer et al.
A star can help probe Einstein’s general relativity theory close to a black hole that is 4 million times as massive as the Sun.

87  Imaging the Homogeneous Nucleation During the Melting of Superheated Colloidal Crystals
Z. Wang et al.
Uniform colloidal crystals are used to study the effects of superheating on homogeneous melting.
>> Perspective p. 55

90  A Local Proton Source Enhances CO₂ Electroreduction to CO by a Molecular Fe Catalyst
C. Costentin et al.
Phenol groups in an iron complex appear to facilitate catalysis of carbon dioxide reduction by supplying protons.

94  Dynamics of DNA Supercoils
M. T. J. van Loenhout et al.
The movement of intertwined loops, or plectonemes, along a twisted DNA molecule was visualized.
>> Perspective p. 56

98  Complex Dental Structure and Wear Biomechanics in Hadrosaurid Dinosaurs
G. M. Erickson et al.
The teeth in duck-billed dinosaurs were as functionally refined as those of present-day mammals.
>> Science Podcast

101  Rapid Acceleration Leads to Rapid Weakening in Earthquake-Like Laboratory Experiments
J. C. Chang et al.
High-velocity experiments simulate slip along a fault patch during a large earthquake.
>> Perspective p. 54

105  The Efficacy of Student-Centered Instruction in Supporting Science Learning
E. M. Granger et al.
A randomized trial reveals that opportunities to support models with evidence aids understanding in grade-school students.

108  Wnt5a Potentiates TGF-β1 Signaling to Promote Colonic Crypt Regeneration After Tissue Injury
H. Miyoshi et al.
Repair of the intestinal epithelium requires both cell proliferation and replacement of crypt stem cells.
>> Perspective p. 51

113  Insect Herbivores Drive Real-Time Ecological and Evolutionary Change in Plant Populations
A. A. Agrawal et al.
Protecting the common evening primrose from being eaten by insects alters its phenotype in only five growing seasons.

116  Natural Enemies Drive Geographic Variation in Plant Defenses
T. Züst et al.
A field study demonstrates that specialist aphid feeders cause changes in the defenses mounted by plants.
>> Perspective p. 50

120  Intestinal Inflammation Targets Cancer-Inducing Activity of the Microbiota
J. C. Arthur et al.
Microbes resident in the gut can promote colorectal cancer in mice in an inflammation-independent manner.
>> Perspective p. 52

124  BDNF Is a Negative Modulator of Morphine Action
J. W. Koo et al.
Morphine reward is modulated by ventral tegmental area brain-derived neurotrophic factor in a way that is opposite to its modulation of cocaine reward.

128  Shared Synaptic Pathophysiology in Syndromic and Nonsyndromic Rodent Models of Autism
S. J. Baudouin et al.
Deficiency or mutation of the postsynaptic adhesion protein neurexin-3 may contribute to cognitive defects in autism.

132  In Monkeys Making Value-Based Decisions, LIP Neurons Encode Cue Salience and Not Action Value
M. L. Leathers and C. R. Olson
Parietal cortex neurons respond to cues that predict large penalties as well as large rewards.

135  Network Resets in Medial Prefrontal Cortex Mark the Onset of Behavioral Uncertainty
M. P. Karlsson et al.
Abrupt neuronal activity in the rat prefrontal cortex indicates a switch from exploitation to exploration.

CONTENTS continued >>
Efficient Hybrid Solar Cells Based on Meso-Superstructured Organometal Halide Perovskites
M. M. Lee et al.
10.1126/science.1228604

Offspring from Oocytes Derived from in vitro Primordial Germ Cell–like Cells in Mice
K. Hayashi et al.
10.1126/science.1226889

IRE1α Cleaves Select microRNAs During ER Stress to Dererepress Translation of Proapoptotic Caspase-2
J.-P. Upton et al.
10.1126/science.1226191

Elfn1 Regulates Target-Specific Release Probability at CA1-Interneuron Synapses
E. L. Sylwestrak and A. Ghosh
10.1126/science.1224842

Intramitochondrial Transport of Phosphatidic Acid in Yeast by a Lipid Transfer Protein
M. Connerth et al.
10.1126/science.1225625

RESEARCH ARTICLE: An Interaction Between BZR1 and DELLAs Mediates Direct Signaling Crosstalk Between Brassinosteroids and Gibberellins in Arabidopsis
Q.-F. Li et al.

DELLA transcription factors mediate crosstalk between two pathways that control plant growth.

PERSPECTIVE: HCN1 Channels—A New Therapeutic Target for Depressive Disorders?
M. M. Shah

Inhibition of hyperpolarization-activated cyclic nucleotide-gated channels may relieve depression.

PERSPECTIVE: Factors Contribute to Depression and Its Comorbid Conditions
H. Anisman and S. Hayley

Manipulation of pro- and anti-inflammatory mediators may improve treatments for depression.

>> Depression section p. 67

PRESENTATION: Circadian Rhythms of Glucocorticoid Hormone Actions in Target Tissues—Potential Clinical Implications
T. Kino

The circadian clock helps to determine tissue sensitivity to glucocorticoids.

PRESENTATION: Primary Generalized Glucocorticoid Resistance and Hypersensitivity—The End-Organ Involvement in the Stress Response
E. Charmandari

The distinct activities of glucocorticoid receptor variants may affect glucocorticoid therapy.

RESEARCH ARTICLE: A Translational Paradigm for the Preclinical Evaluation of the Stroke Neuroprotectant Tat-NR2B9c in Gyrencephalic Nonhuman Primates
D. J. Cook et al.

Primates treated with a neuroprotectant after stroke showed outcomes that mimicked those of a human trial.

RESEARCH ARTICLE: Prevention of Alveolar Destruction and Airspace Enlargement in a Mouse Model of Pulmonary Lymphangioleiomyomatosis (LAM)
E. A. Goncharova et al.

Rapamycin and simvastatin treatment of a mouse model of pulmonary lymphangioleiomyomatosis is described.

RESEARCH ARTICLE: Rapid Whole-Genome Sequencing for Genetic Disease Diagnosis in Neonatal Intensive Care Units
C. J. Saunders et al.

Rapid whole-genome sequencing of neonates can shorten time to disease diagnosis and counseling.

COMMENTS

“Rape in the University: The Dark Side of Higher Education”
D. J. Cook et al.

Graduate students’ pressures make them especially prone to depression, but small changes can help.

>> Depression section p. 67

Taken for Granted: America’s Real Jobs Gap
B. L. Benderly

A new book solves the mystery of America’s employment situation and tells how to fix it.

A Career for Two, With Empathy
E. Pain

A husband-and-wife team studies the brain areas that allow us to feel what others feel.

>> Depression section p. 67

Depression resilience, properties of dinosaur teeth, mysteries of the brain, and more.