

nature insight

Obesity



Cover and side panel illustration

Coloured scanning electron micrograph of fat cells (orange) surrounded and supported by connective tissue fibres (brown) in human adipose connective tissue. (Images courtesy of Quest/SPL.)

We are all familiar with the term ‘obesity’, but few of us see it as a real disease. The large and manipulative diet industry characterizes obesity as arising from a lack of self-control, and this is a widely held belief. In fact, obesity is a complex disorder of appetite regulation and energy metabolism controlled by specific biological factors. Genes that predispose to obesity in humans and animals have already been identified and indicate the importance of genetic factors in the development of disease.

Five years ago, leptin was identified as the protein responsible for suppressing appetite. It was hailed as a potential wonder drug and catapulted obesity research to the forefront of biomedical science and public imagination. Yet today, in the developed world the incidence of obesity is rising, and there are now as many obese people in the world as there are people suffering from hunger. The financial burden, health risks and impact on quality of life associated with this epidemic warrant a detailed understanding of the molecular mechanisms that regulate body weight, in order to identify new treatments. We therefore devote this collection of reviews — the first in a new, regular feature called ‘*Nature Insight*’ — to the molecular biology of obesity.

An overview of the topic is provided by Jeff Friedman on page 632, who with co-workers identified leptin in 1995. (A special news feature on pages 538–540 of this issue examines just how well leptin has lived up to its therapeutic promise.) Obesity has now replaced undernutrition and infectious disease as the most significant contributor to ill health, and Peter Kopelman examines the epidemiology of obesity and its associated medical problems on page 635. The discovery of mutations in human and model organisms, and complementary studies of populations, provide fundamental insight into the primary cause of the disease and are described by Greg Barsh and co-workers on page 644. The thermodynamics of energy expenditure in the mitochondrion and the mechanism of transcriptional control of mitochondrial genes are examined on page 652 by Bradford Lowell and Bruce Spiegelman. Key signalling molecules involved in the hormonal regulation of metabolism by neuronal circuits in the hypothalamus are highlighted by Michael Schwartz and co-workers on page 661, providing insights into energy homeostasis at the molecular level. Finally, when prevention fails, what drugs are available to treat obesity? Although there seems no real cure as yet, on page 672 George Bray and Louis Tartaglia discuss current treatment strategies which aim to inhibit food intake and block fat digestion and provide knowledge of therapeutic agents on the horizon.

We are pleased to acknowledge the financial support of The Roche Group in producing this *Nature Insight*. We share interest and enthusiasm for the advances made in the treatment of obesity. Of course, *Nature* carries the sole responsibility for all editorial content and rigorous peer-review to our normal high standards.

By exploring this disease from its basic epidemiology and associated health risks, through to the molecular mechanisms for regulation and possible therapeutic intervention that may exist, we hope that there is something to be gained by the basic scientist, clinician and the general reader.

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