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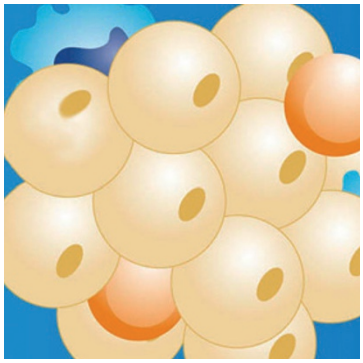
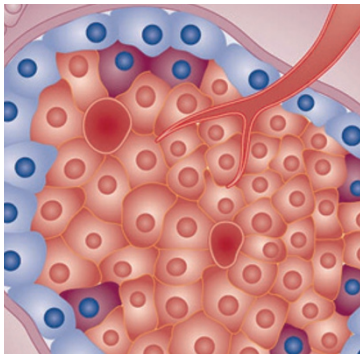


Obesity-associated inflammation



Therapeutically increasing pancreatic β-cell mass and function

Clinical trials of potential novel anxiolytic agents have been disappointing, despite promising findings from extensive preclinical research efforts on these agents. In their Review, Griebel and Holmes analyse the major trends from a comprehensive database of published preclinical studies on novel anxiolytic agents in the past 50 years. Key issues that might have hampered their progress and recommendations for how to improve future anxiolytic drug discovery are discussed. Meanwhile, Hetz and colleagues discuss how the accumulation of unfolded or misfolded proteins inside the endoplasmic reticulum (ER) can lead to cellular stress and contribute to disease. They provide an overview of the role of the unfolded protein response (UPR) in restoring protein-folding homeostasis within the ER and review recent advances in targeting the UPR using pharmacological and gene therapy approaches in neurodegenerative and metabolic disorders, cancer and inflammation. Sphingosine-1-phosphate (S1P; a bioactive lipid involved in numerous cellular functions, including the control of immune cell trafficking) has been implicated in several disorders, particularly cancer and inflammatory diseases. In their Review, Spiegel and colleagues discuss strategies to therapeutically target the generation, transport and degradation of S1P, as well as S1P cell-surface receptors, and highlight agents currently in clinical trials. Finally, this month we are featuring two posters illustrating emerging approaches for the treatment of diabetes: one focusing on the potential of targeting obesity-associated inflammation, the other presenting strategies to therapeutically increase pancreatic β-cell mass and function. The posters were produced with exclusive support from Novo Nordisk and are freely available at http://www.nature.com/nrd/posters/index.html. As always, Nature Publishing Group carries sole responsibility for all editorial content.

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