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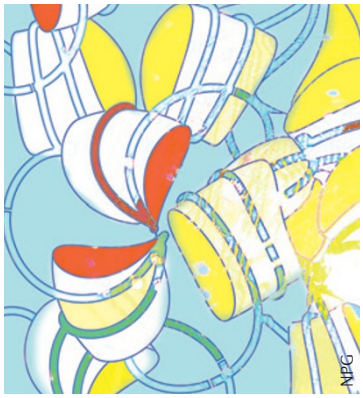

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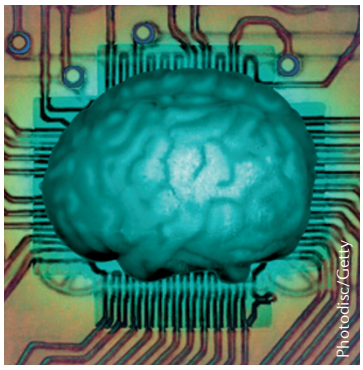

Neuropeptide receptors and psychiatric diseases p462

The finding that caloric restriction slows ageing and delays disease onset in several species has stimulated interest in understanding the molecular mechanisms underlying these beneficial effects and in developing pharmacological agents that are capable of mimicking such dietary intervention. One of the most intriguing molecules to emerge from such studies is the NAD-dependent deacetylase sirtuin 1 (SIRT1), which is thought to have a role in age-related conditions including diabetes, cardiovascular disease, neurodegenerative disorders and cancer. Baur and colleagues discuss some of these roles and the potential of SIRT1 as a drug target, including the recent controversies surrounding the mechanism of action of SIRT1 activators. Fragmented understanding of the mechanisms of metastasis — which is responsible for most of the deaths from solid cancers — has hampered the identification of drugs with anti-metastatic efficacy. However, substantial progress has been recently made in the development of preclinical models and the identification of genes that regulate metastasis or act as biomarkers. Focusing on breast cancer, Anderson and colleagues discuss how such knowledge could be applied in the discovery and development of novel anti-metastatic therapies. Knowledge of relevant biomarkers could help address the heterogeneity among patients in clinical trials for psychiatric diseases such as depression and schizophrenia; this has been a major factor in the failure of efforts to develop novel drugs targeting various neuropeptide receptors. This is discussed by Griebel and Holsboer, who analyse the discrepancy between the highly promising preclinical data and the unsuccessful clinical trials for several classes of neuropeptide receptor modulators, suggesting new ways to exploit their full potential.

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