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JAPAN: nature@naturejpn.com
Rinoko Asami, Nature Japan KK
Tel: +81 3 3267 8751; Fax: +81 3 3267 8746

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One of the most exciting findings in drug discovery targeted at G-protein-coupled receptors (GPCRs) is that these receptors are not simple on/off switches, which means that drugs can be designed to induce 'textured responses' to stabilize receptors in conformations that participate in some, but not all, of the receptor's complex repertoire of behaviours. In this issue, Kenakin explores the concepts of 'collateral efficacy' and 'permissive antagonism' in the search for GPCR modulators with unique therapeutic profiles. Another highly complex issue is combinatorial pharmacogenetics, a discipline that seeks to characterize the effects of multiple genetic variations on drug responses. Wilke and colleagues discuss novel analysis techniques, such as multifactor dimensionality reduction, for evaluating pharmacogenetic data, which could facilitate the development of improved gene-based dosing models to allow safer drug prescribing. Several articles in this issue focus on important therapeutic areas. Page and Roden summarize current and future drugs for the treatment of atrial fibrillation, a condition that is associated with increased incidence of heart disease and mortality. De Clercq and Holy present a 'Case history' — the discovery and development of acyclic nucleoside phosphonates, which have had a significant impact on our ability to treat several major viral diseases. For the battle against infectious bacteria, Nathan and Goldberg suggest strategies to stimulate the much-needed development of new antibiotics, an area from which much of the pharmaceutical industry has withdrawn from R&D owing to the lack of potential for return on investment. Finally, Chin-Dusting and colleagues investigate the role of academic–industrial collaborations for finding improved medicines, and debate the value of these partnerships and different models for such collaborations.


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