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► **COVER:** 'Keys to new doors in drug discovery targeting seven-transmembrane receptors' inspired by the perspective on p617.



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Seven-transmembrane (7TM) receptors continue to represent one of the most popular classes of drug targets, but the cellular assays that are commonly used to identify ligands may not capture the complexities of 7TM receptor activation and signalling.

In his Perspective, Kenakin discusses how the apparent efficacy of drugs that act at 7TM receptors is linked to the particular pharmacological assay used and suggests that a return to whole-system assays may lead to the identification of agents that have greater specificity and efficacy. Our Reviews this month cover a range of topics. A hallmark of many human cancers is aberrant activity of the phosphoinositide 3-kinase (PI3K) pathway. Although targeting specific components of this pathway is proving to be a promising therapeutic strategy, several key challenges have recently emerged. In their Review, Liu and colleagues discuss current targets and agents that are under investigation, focusing on approaches to overcome the complications associated with feedback loops, pathway crosstalk and the development of resistance. Other promising therapeutic targets for various cancers include selectins — members of the lectin family of carbohydrate-binding proteins, which recognize and mediate the biological effects of carbohydrates. Ernst and Magnani discuss the potential and challenges for therapeutically targeting carbohydrate-binding proteins, and review recent preclinical research that supports the use of small-molecule glycomimetics as a novel class of agents for the treatment of disorders including cancer, and infectious and inflammatory diseases. Finally, Akdis and Akdis review mechanisms of immune tolerance and allergic inflammation, and highlight recent advances in the development of long-term allergen-specific strategies that target T cell responses in the treatment of allergy and chronic inflammatory disorders such as asthma.

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