

nature REVIEWS

NATURE REVIEWS DRUG DISCOVERY

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In the wake of recent highly publicized drug withdrawals, several articles in this issue focus on problems in drug discovery and development, and ways to improve the process in a cost-effective manner. On the 'Analyst's couch', Melnikova looks at the rapid rise and even more rapid demise of COX2 inhibitors that sent shock waves through the stock market in 2004. Steinman describes the 'Case history' of natalizumab, a promising new therapeutic antibody for the treatment of multiple sclerosis that was approved in November 2004, but withdrawn from the market in February 2005 due to serious adverse effects. Kaplowitz addresses the issue of idiosyncratic drug hepatotoxicity, which is the most frequent cause of post-marketing warnings and withdrawals. As pharmacogenomic testing offers the potential of reducing drug-related adverse events, Phillips and Van Bebber consider how economics-based resource-allocation frameworks can be used to assess the value of such tests from a population perspective. Focusing on novel approaches to drug discovery, Butcher argues that real advances in medicine must include the generation of drugs that act through novel mechanisms. This perspective analyses the question of whether cell systems biology can rescue drug discovery, and compares and contrasts this approach with the current target-based drug discovery paradigm. Spedding and co-workers propose a hypothesis-driven, systems-level approach to drug discovery and development for psychiatric disease, and discuss genomics-based and alternative screening approaches. Finally, Dube and Bertozzi review glycans associated with cancer and inflammation, and new therapeutic and diagnostic strategies that are based on the underlying glycobiochemistry.



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