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► **COVER:** 'Dawn of the next generation of mTOR inhibitors' by Susanne Harris, inspired by the Review on p868.



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Using biomarkers to identify subsets of patients who are likely to benefit from a given therapy has the potential to substantially improve patient care and reduce the size, cost and failure rates of clinical trials. However, coordinating the co-development of a drug with a diagnostic to produce such a 'stratified medicine' is challenging. With this in mind, a group from academia, industry and the US Food and Drug Administration present extensive computational analyses, based on real-life case studies in oncology and Alzheimer's disease, that quantify the effects of key factors such as clinical trial design and predictive biomarker prevalence on the economic value of stratified medicines. Alzheimer's disease exhibits remarkable similarities to Huntington's disease at the level of molecular pathogenic processes. In their Review, Hayden and colleagues discuss common therapeutic targets within these shared pathways that could be exploited for drug development. Age-related diseases such as Alzheimer's disease are among the disorders in which dysregulated mammalian target of rapamycin (mTOR) signalling has been implicated. Hall and colleagues review the roles and functions of mTOR signalling in health and disease, including cancer and metabolic disorders. They consider reasons why the allosteric mTOR inhibitors rapamycin and its analogues have not met clinical expectations, and discuss the therapeutic potential of a new generation of ATP-competitive mTOR inhibitors that are in early-stage clinical trials for cancer. Although originally only used in cancer therapy, the potential use of nanomedicine in the management of atherosclerosis is now also emerging. In a final Review, Mulder and colleagues discuss recent advances in the application of nanoparticle technology in the diagnosis and treatment of atherosclerosis.

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