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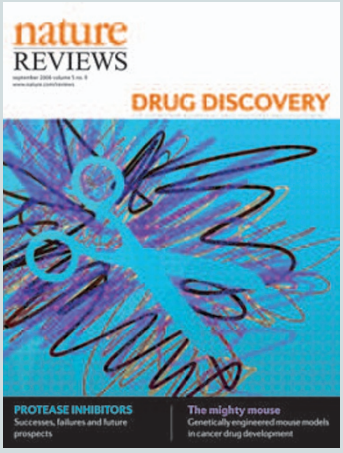


► **COVER:** 'Signalling scissors: proteases as targets' by Susanne Harris, inspired by the review on p785.


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Can an open-source research help address the biopharma industry's seemingly ever-present problems of rising R&D costs and declining innovation? This month, an Outlook article by Munos considers this question, highlighting how drug R&D might benefit from insights and strategies from the open-source model pioneered by the software industry in the 1990s. Positive examples are provided by public–private partnerships (PPPs) that have been established to tackle neglected diseases, where open-source is combined with outsourcing to create a novel low-cost business model. Meanwhile, Copeland and colleagues consider how to take a much older insight from Paul Ehrlich — that a drug will not work unless it is bound to its molecular target — to another level. The authors propose that a key factor is not the apparent affinity of the drug for its target *per se*, but rather the residence time of the drug on its molecular target, providing an additional parameter for compound optimization. Another field in need of optimization is the development of animal models, and Sharpless and DePinho discuss the shortcomings of current xenograft mouse models for cancer and the opportunities and challenges presented by novel genetically engineered mouse models for evaluating new cancer therapies. The anticancer activities of a promising new class of such therapies — histone deacetylase inhibitors — are discussed by Bolden and colleagues; these agents not only affect epigenetic changes in cancer cells, but also seem to inhibit neoplastic growth and survival by regulating host immune response and tumour vasculature. Finally, in two further reviews, drug targets with potential for a whole spectrum of diseases are discussed. Turk looks at successes, failures and future prospects of protease research, and Evgenov and colleagues explore the potential of targeting soluble guanylate cyclase, a key signalling molecule activated by nitric oxide.


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