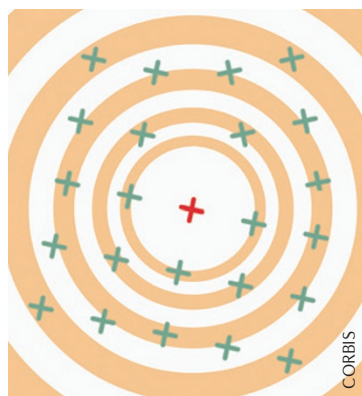


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The therapeutic index of drug candidates — a quantitative relationship between indicators of their safety and efficacy — is a concept that is widely used to aid the identification of candidates that have an appropriately balanced risk–benefit profile for a given indication. In their Perspective, Muller and Milton discuss key issues associated with the determination and interpretation of therapeutic indices during different stages of the development process. Meanwhile, our Reviews this month cover an array of topics. Miossec and Kolls discuss the physiological and pathological roles of interleukin-17 (IL-17), a pro-inflammatory cytokine produced by a subset of helper T cells termed T_H17 cells. They present recent advances in targeting the IL-17–T_H17 pathway in the treatment of several chronic inflammatory disorders while considering the associated challenges and limitations. Inflammation is among the many biological processes in which the transforming growth factor- β (TGF β) signalling pathway has a key role. Akhurst and Hata provide an overview of the mechanisms of TGF β signalling and discuss strategies for therapeutically intervening in the pathway. Clinical trials of agents currently under development for the treatment of a variety of disorders, including cancer, fibrosis and scleroderma, are discussed. Finally, Raju, Goldberg and Rubin discuss the therapeutic potential of targeting the bacterial degradative proteases, which have important roles in key processes such as the regulation of stress responses, cellular replication and division, and virulence. They focus on those proteases that represent the most appealing therapeutic targets, highlighting recent advances and challenges in developing modulators of these enzymes as novel antibacterial agents.

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