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Oncology is one of the most active therapeutic areas, and three Reviews this month describe different pathways that could be targeted to treat cancer, as well as other diseases. Histone modifications alter the cellular transcriptional profile, and dysregulation of histone acetylation frequently occurs in cancer. These modifications are 'read' by proteins with bromodomains, including those from the bromodomain and extra-terminal (BET) family. In their Review, Filippakopoulos and Knapp discuss BET bromodomain inhibitors and preclinical studies of their therapeutic potential for cancer, inflammation and viral infections. In the second Review, Andersson and Lendahl consider therapeutic opportunities in the Notch pathway, which was discovered a century ago in *Drosophila melanogaster*. As well its key role in development, this evolutionarily conserved pathway is important in maintaining homeostasis in many adult tissues, and so determining how and where to intervene will be critical in the development of Notch-centred therapeutics with acceptable safety profiles. The authors analyse the potential use of Notch pathway inhibitors to treat diseases including cancer and those of the vasculature system, and discuss how crosstalk between Notch and other signalling pathways could provide opportunities to develop combination therapies. Finally, Spolski and Leonard focus on intervention in interleukin-21 (IL-21) signalling; IL-21 is a cytokine that was discovered at the start of this century and regulates both innate and adaptive immune responses. Depending on the context, either blockade or enhancement of IL-21 signalling could be desirable; clinical trials of IL-21 itself as an immune reactivator for the treatment of solid tumours are in progress, and IL-21-blocking agents are being clinically investigated for autoimmune diseases.

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