IN BRIEF

ANEUPLOIDY

Lack of a full set is damaging

Whole chromosomal instability (CIN) is known to contribute to aneuploidy, but can it also cause DNA damage? In cells in which aneuploidy is promoted by a drug that induces incorrect kinetochore attachment, and hence lagging chromosomes at mitosis, sites of DNA damage and chromosomal rearrangements are increased. Chromosomes that are incorrectly segregated are often damaged during cytokinesis, and the resulting DNA double-strand breaks trigger an ataxia telangiectasia mutated (ATM)–CHK2–p53-mediated DNA damage response. These data further imply that CIN actively contributes to genomic instability and potentially to a tumorigenic phenotype.

ORIGINAL RESEARCH PAPER Janssen, A. *et al.* Chromosome segregation errors as a cause of DNA damage and structural chromosomal aberrations. *Science* **333**, 1895–1898 (2011)

THERAPY

Wager of war on bromodomains

Dawson and colleagues showed that mixed-lineage leukaemia (MLL) fusion proteins, which commonly occur in aggressive leukaemia, associate with the bromodomain and extraterminal (BET) family of chromatin adaptor proteins. So, to target MLL-fusion-induced transcriptional responses, the authors treated mouse and human MLL-fusion leukaemia cells with a BET inhibitor, GSK1210151A, which induced cell cycle arrest and apoptosis. GSK1210151A treatment altered the expression of a common set of genes; in particular, *BCL2*, *MYC* and cyclin-dependent kinase 6 (*CDK6*) expression was reduced. The drug also improved the survival of mice with leukaemia induced by the expression of MLL-AF9 or MLL-AF4. In another paper, Mertz and colleagues treated various leukaemia and lymphoma cell lines with the BET inhibitor JQ1, which suppressed *MYC* expression and altered the expression of MYC target genes. Treatment with JQ1 resulted in cell cycle arrest and apoptosis, which was suppressed by exogenous expression of *MYC* from a BET regulation-resistant promoter. Finally, JQ1 reduced tumour growth of Burkitt's lymphoma cell and acute myeloid leukaemia cell xenografts. Together, these and the other recent papers that have investigated targeting the BET family indicate that this could be an efficacious strategy for targeting several types of leukaemia and, potentially, tumours overexpressing MYC.

ORIGINAL RESEARCH PAPERS Dawson, M. A. *et al.* Inhibition of BET recruitment to chromatin as an effective treatment for MLL-fusion leukaemia. *Nature* 2 Oct 2011 (doi:10.1038/nature10509) | Mertz, J. A. *et al.* Targeting MYC dependence in cancer by inhibiting BET bromodomains. *Proc. Natl Acad. Sci. USA* 26 Sep 2011 (doi:10.1073/pnas.1108190108)

BREAST CANCER

Suppressing a resistant population

Luminal breast cancers, which are oestrogen receptor (ER) and/or progesterone receptor (PR) positive, typically respond well to hormone therapies, but resistance and tumour recurrence can occur. Haughian *et al.* show that more than half of primary ER^+PR^+ tumours also contain a subpopulation of 'luminobasal' cells that are ER^-PR^-. In xenograft models of luminal tumours, ER^-PR^- cells expanded in response to hormone therapies. Expansion depended on NOTCH1 signalling and could be blocked by γ-secretase inhibitors, which may help to overcome hormone therapy resistance.

ORIGINAL RESEARCH PAPER Haughian, J. M. *et al.* Maintenance of hormone responsiveness in luminal breast cancers by suppression of Notch. *Proc. Natl Acad. Sci. USA* 3 Oct 2011 (doi:10.1073/pnas.1106509108)