IN BRIEF

ANTICANCER DRUGS

Decoy receptor prevents metastasis

AXL receptor tyrosine kinase signalling drives metastasis and disease progression in a number of human cancers, representing a promising oncology target. However, attempts to therapeutically target the AXL receptor have been limited by modest antitumour efficacy and substantial off-target effects. Now, Kariolis *et al.* have engineered an AXL decoy receptor, MYD1 Fc, which binds the AXL ligand GAS6 with high affinity, efficiently reducing GAS6-mediated AXL phosphorylation and downstream signalling. In mouse models of advanced ovarian and breast cancer, MYD1 Fc potently inhibited metastasis and disease progression, an effect which correlated with GAS6 affinity.

ORIGINAL RESEARCH PAPER Kariolis, M. S. *et al.* An engineered Axl 'decoy receptor' effectively silences the Gas6-Axl signaling axis. *Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.1636 (2014)

CANCER

Predicting synthetic lethal interactions

Harnessing synthetic lethality — which occurs when the inhibition of two non-essential genes is lethal — is attracting significant attention as a strategy to selectively treat cancer. Here, the authors use the data mining synthetic lethality identification pipeline (DAISY) to analyse the accumulating cancer genomic data. They construct a genome-wide network of synthetic lethality interactions in cancer, which they demonstrate to successfully predict gene essentiality, drug efficacy and clinical prognosis.

ORIGINAL RESEARCH PAPER Jerby-Arnon, L. *et al.* Predicting cancer-specific vulnerability via data-driven detection of synthetic lethality. *Cell* **158**, 1199–1209 (2014)

DRUG DESIGN

Increasing stability of ADCs

Interest in the use of antibody–drug conjugates (ADCs) for cancer therapy has increased recently, with two approved for clinical use. However, issues with the *in vivo* stability of the linkers used in many ADCs — based on maleimide-containing components conjugated to reactive thiols — have become apparent. To address this, Lyon *et al.* incorporated a basic functional group adjacent to the maleimide, which induced the thiosuccinimide ring to undergo rapid hydrolysis, protecting it from maleimide elimination reactions. This 'self-stabilizing' ADC exhibited improved antitumour activity and reduced bone marrow toxicity in mouse lymphoma xenograft models.

ORIGINAL RESEARCH PAPER Lyon, R. P. *et al.* Self-hydrolyzing maleimides improve the stability and pharmacological properties of antibody-drug conjugates. *Nature Biotechnol.* http://dx.doi.org/10.1038/nbt.2968 (2014)

INFECTIOUS DISEASE

Durable protection against Ebola virus

Human-derived replication-defective adenovirus (rAd) vectors have been successfully used to generate protective immunity against acute lethal Ebola virus (EBOV; previously known as Zaire ebolavirus) challenge in rhesus macaques, but their use is limited by pre-existing vector immunity. Here, Stanley *et al.* describe the development of a vaccine comprised of a chimpanzee-derived rAd (ChAd3) that encodes EBOV glycoprotein. Rhesus macaques administered a single dose of the vaccine were protected from an acute EBOV challenge 5 weeks later, and when boosted with a second vaccine — modified vaccinia Ankara expressing EBOV glycoprotein — were still protected at 10 months.

ORIGINAL RESEARCH PAPER Stanley, D. A. *et al.* Chimpanzee adenovirus vaccine generates acute and durable protective immunity against ebolavirus challenge. *Nature Med.* http://dx.doi.org/10.1038/nm.3702 (2014)