IN BRIEF

ADVERSE DRUG REACTIONS

Computational model predicts side effects

This paper used computational methods based on chemical structural similarity to predict the off-target activity of 656 marketed drugs against 73 protein targets. About 600 of the ~900 predictions were then tested experimentally, and around 50% were found to be genuine. For example, the methods predicted that the non-steroidal synthetic oestrogen chlorotrianisene (which is linked to abdominal pain) had potent affinity for cyclooxygenase 1 (an enzyme found in gastric mucosa); this prediction was confirmed using an *ex vivo* assay. So this model can detect previously unappreciated side effects, albeit with a high false-positive rate.

ORIGINAL RESEARCH PAPER Lounkine, E. *et al.* Large-scale prediction and testing of drug activity on side-effect targets. *Nature* **486**, 361–367 (2012)

PSYCHIATRIC DISORDERS

Targeting a PI3K subunit in schizophrenia

Genetic variations in the growth factor neuregulin 1 (NRG1) and in its receptor tyrosine kinase ERBB4 are associated with an increased risk of schizophrenia. Law *et al.* identified a signalling pathway regulated by schizophrenia-associated ERBB4 genotype, which involved increased expression of a phosphoinositide 3-kinase (PI3K)-linked ERBB4 receptor and the PI3K subunit p110δ. In rodent models, inhibition of p110δ using a small molecule prevented psychosis and reversed schizophrenia-related phenotypes, suggesting that p110δ could be a new target for the treatment of schizophrenia.

ORIGINAL RESEARCH PAPER Law, A. J. *et al.* Neuregulin 1–ErbB4–PI3K signaling in schizophrenia and phosphoinositide 3-kinase–p110δ inhibition as a potential therapeutic strategy. *Proc. Natl Acad. Sci. USA* 11 Jun 2012 (doi:10.1073/pnas.1206118109)

OBESITY AND DIABETES

Adenosine pathway increases β-cell regeneration

This study screened ~7,000 small molecules in a zebrafish model of diabetes to identify compounds that enhanced β-cell regeneration. Four of the identified compounds were modulators of the adenosine signalling pathway. The most potent enhancer of β-cell regeneration (but not of normal development) was the adenosine receptor agonist 50-*N*-ethylcarboxamidoadenosine, which had glucose-lowering effects in zebrafish and diabetic mice. So, targeting the adenosine pathway could be a therapeutic option in diabetes.

ORIGINAL RESEARCH PAPER Andersson, O. *et al.* Adenosine signaling promotes regeneration of pancreatic β cells *in vivo*. *Cell Metabol.* **15**, 885–894 (2012)

ANTICANCER DRUGS

Synthetic lethality enables targeting of MYC

MYC oncogenes are implicated in various cancers, but are considered difficult to 'drug' as they encode transcription factors. Toyoshima *et al.* used a functional genomic screen to identify genes that, when expressed with oncogenic MYC, provide a synthetic lethal interaction. Several genes were identified that selectively induced the accumulation of DNA damage in MYC-expressing cells. Validation studies showed that inhibition of casein kinase 1ε, expression of which correlated with MYC expression in human cancers, prevented the growth of MYC-amplified neuroblastoma xenografts.

ORIGINAL RESEARCH PAPER Toyoshima, T. *et al.* Functional genomics identifies therapeutic targets for MYC-driven cancer. *Proc. Natl Acad. Sci. USA* **109**, 9545–9550 (2012)