IN BRIEF

MELANOMA

Directed therapy

This paper shows that treatment of melanoma cells with methotrexate (an inhibitor of dihydrofolate reductase (DHFR)) induces the expression of microphthalmia-associated transcription factor (MITF). MITF induces melanocyte differentiation by inducing the transcription of genes, such as tyrosinase (*TYR*), and inhibits invasive growth. Expression of TYR enables the activation of a prodrug, 3-*O*-(3,4,5-trimethoxybenzoyl)-(–)-epicatechin (TMECG), which also inhibits DHFR. Combined treatment of melanoma cells with methotrexate and TMECG depletes thymidine pools and induces DNA damage and apoptosis *in vivo*.

ORIGINAL RESEARCH PAPER Sáez-Ayala, M. *et al.* Directed phenotype switching as an effective antimelanoma strategy. *Cancer Cell* http://dx.doi.org/10.1016/j.ccr.2013.05.009 (2013)

MATHEMATICAL MODELS

Two or three is better than one

Resistance to targeted therapies is commonplace, so should we use more than one drug and target different pathways? Martin Nowak and colleagues built a mathematical model to address this question. They used lesion regression and growth data from 20 patients with metastatic melanoma who were treated with vemurafenib to generate the model parameters. They then applied the model to independent data sets from patients with metastatic disease. According to the model, dual therapy with two hypothetical drugs that target two different pathways would result in long-term control, as long as there are no single mutations that produce cross-resistance to both drugs. Patients with substantial disease burden would require three or more drugs for long-term benefit. Moreover, the model shows that combined rather than sequential treatment is far better.

ORIGINAL RESEARCH PAPER Bozic, I. *et al.* Evolutionary dynamics of cancer in response to targeted combination therapy. *eLIFE* **2**, e00747 (2013)

CANCER MODELS

Getting it right

A comparison of genomic data from 47 ovarian cancer cell lines with serous ovarian cancer data from The Cancer Genome Atlas showed substantial differences between commonly used ovarian cancer cell lines and this cancer type. Several rarely used cell lines more closely resemble the human disease and therefore seem to be more suitable cell line models.

ORIGINAL RESEARCH PAPER Domcke, S. *et al.* Evaluating cell lines as tumour models by comparison of genomic profiles. *Nature Comm.* http://dx.doi.org/10.1038/ncomms3126 (2013)

GLIOBLASTOMA

Branching out

Branched-chain amino acid transaminase 1 (BCAT1), an enzyme that triggers the catabolism of branched-chain amino acids, is overexpressed in glioblastomas with wild-type isocitrate dehydrogenase 1 (*IDH1*) and *IDH2*. The activity of BCAT1 in human astrocytes is inhibited in the presence of mutant IDH1, and suppression of BCAT1 activity in IDH-wild-type glioma cell lines inhibited the excretion of glutamate, leading to reduced proliferation and invasiveness *in vitro* and reduced growth of glioblastoma xenografts *in vivo*.

ORIGINAL RESEARCH PAPER Tönjes, M. *et al.* BCAT1 promotes cell proliferation through amino acid catabolism in gliomas carrying wild-type IDH1. *Nature Med.* http://dx.doi.org/10.1038/nm.3217 (2013)