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IN BRIEF

CANCER

Targeting telomeres

Telomere maintenance enables the indefinite proliferation potential of cancer cells and is among the most frequent alterations in human glioblastoma (GBM). Here, Bejarano *et al.* report that expression of the telomere binding protein TRF1 — essential for telomere capping and protection — is upregulated in mouse and human GBM compared with normal brain tissue. In mouse GBM models, *Trf1* deletion increased telomeric damage, reduced stemness and inhibited GBM initiation and progression. Small-molecule TRF1 inhibitors mimicked these anticancer effects in patient-derived human xenografts.

ORIGINAL ARTICLE Bejarano, L. *et al.* Inhibition of TRF1 telomere protein impairs tumor initiation and progression in glioblastoma mouse models and patient-derived xenografts. *Cancer Cell* **32**, 590–607 (2017)

IMMUNOTHERAPY

Vaccine patch to treat melanoma

The use of whole tumour cell preparations in cancer immunotherapy, to simultaneously target multiple tumour antigens to activate the immune response, is a promising therapeutic approach. Ye *et al.* have developed a transdermal microneedle vaccine patch that directly targets antigen-presenting cells via delivery of B16F10 melanoma whole tumour lysates combined with melanin. Application of the patch in conjunction with near-infrared irradiation — which melanin transforms to heat, which boosts the immune response — prevented tumour engraftment in prophylactic mouse melanoma models and caused sustained tumour regression in mice with established tumours.

ORIGINAL ARTICLE Ye, Y. *et al.* A melanin-mediated cancer immunotherapy patch. *Sci. Immunol.* **2**, eaan5692 (2017)

TECHNOLOGY

New method for endogenous protein degradation

Current strategies to modulate protein expression rely on DNA knock out or RNA interference. A novel method — Trim-Away — can directly and rapidly degrade endogenous proteins in mammalian cells, minimizing the risk of phenotype compensation and off-target effects. Trim-Away introduces exogenous TRIM21 (an E3 ubiquitin ligase) and an antibody against the protein of interest into cells via microinjection or electroporation, leading to TRIM21-mediated ubiquitination and degradation by the proteasome. Trim-Away selectively degraded specific proteins in multiple cell types including primary human cells.

ORIGINAL ARTICLE Clift, D. *et al.* A method for the acute and rapid degradation of endogenous proteins. *Cell* **172**, 1692–1706 (2017)

CANCER

Inhibiting DNA damage signalling

The DNA transposase, piggyBac transposable element-derived 5 (PGBD5), is expressed in the majority of childhood solid tumours, where it promotes site-specific genomic rearrangements. Henssen *et al.* hypothesized that PGBD5-expressing cells may depend on active DNA damage repair and signalling for survival. Indeed, cell lines deficient in non-homologous end-joining DNA repair died upon induction of PGBD5 expression. A panel of 19 childhood tumour cell lines was highly sensitive to the DNA damage signalling inhibitor AZD6738, which targets ATR. Oral treatment of mouse tumour models with AZD6738, including patient-derived primary neuroblastoma xenografts, significantly impaired tumour growth without toxicity.

ORIGINAL ARTICLE Henssen, A. *et al.* Therapeutic targeting of PGBD5-induced DNA repair dependency in pediatric solid tumors. *Sci. Transl Med.* **9**, eaam9078 (2017)