IN BRIEF

CANCER

Novel IDH1 mutant inhibitors identified

Point mutations of the isocitrate dehydrogenases IDH1 and IDH2, found in acute myeloid leukaemia (AML), promote a block in cellular differentiation that is due to global DNA hypermethylation. Here, using a high-throughput biochemical screen, Okoye-Okafor *et al.* identify novel allosteric inhibitors of mutant IDH1. In primary IDH1-mutant AML cells and mouse AML xenograft models, the inhibitors decreased production of the IDH1 metabolite 2-hydroxyglutarate, reduced the percentage of blast cells and stimulated myeloid differentiation, also reversing the aberrant DNA hypermethylation patterns induced by mutant IDH1.

ORIGINAL RESEARCH PAPER Okoye-Okafor, U. C. *et al.* New IDH1 mutant inhibitors for treatment of acute myeloid leukemia. *Nat. Chem. Bio.* **11**, 878–886 (2015)

INFLAMMATORY DISORDERS

Blocking periodontal bone loss

Periodontitis is a chronic inflammatory disease that causes destruction of the bone supporting the teeth, and it is often unresponsive to existing treatment. Shin *et al.* demonstrate that developmental endothelial locus 1 (DEL1) — an endothelial cell-secreted protein known to control unwanted inflammatory responses — is also expressed by human and mouse osteoclasts, regulating their differentiation and resorptive function by inhibiting expression of the osteoclastogenic factor nuclear factor of activated T cells cytoplasmic 1 (NFATC1). Locally administered human DEL1 blocked inflammatory bone loss in a monkey periodontitis model.

ORIGINAL RESEARCH PAPER Shin, J. *et al.* DEL-1 restrains osteoclastogenesis and inhibits inflammatory bone loss in nonhuman primates. *Sci. Transl. Med.* **7**, 307ra155 (2015)

OPHTHALMOLOGY

Dual VEGF receptor antagonist reverses retinal disease

Pathological angiogenesis is involved in several severe retinal disorders, including age-related macular degeneration (AMD). Although antibodies targeting the pro-angiogenic factor VEGF have been used to successfully treat AMD, not all patients respond and treatment requires intravitral injection. Now, Sidman *et al.* report that a small cyclic retro-inverted peptidomimetic named Vasotide, which selectively binds to the VEGF receptors VEGFR1 and neuropilin 1, decreases pathological retinal angiogenesis when administered as eye drops to mouse and monkey retinal disease models.

ORIGINAL RESEARCH PAPER Sidman, R. L. *et al.* The peptidomimetic Vasotide targets two retinal VEGF receptors and reduces pathological angiogenesis in murine and nonhuman primate models of retinal disease. *Sci. Transl. Med.* **7**, 309ra165 (2015)

DRUG SCREENING

Identifying novel protein kinase inhibitors

GlaxoSmithKline created the Published Kinase Inhibitor Set (PKIS) — an annotated set of 367 small-molecule kinase inhibitors — to promote research on untargeted protein kinases. Now, Elkins *et al.* provide a comprehensive characterization of PKIS compounds by screening the set against a panel of 224 recombinant kinases and 24 G protein-coupled receptors. Using this information, they develop a selective inhibitor for the previously untargeted kinases LOK and SLK. They also identify cytotoxic and cytostatic compounds in a cancer cell line screen and potential angiogenesis inhibitors in a high-content endothelial tube-formation assay.

ORIGINAL RESEARCH PAPER Elkins J. M. *et al.* Comprehensive characterization of the Published Kinase Inhibitor Set. *Nat. Biotech.* **28**, 370–383 (2015)