IN BRIEF

INFECTIOUS DISEASES

Towards a new class of tuberculosis drugs

The most potent tuberculosis (TB) drug, isoniazid, effectively kills *Mycobacterium tuberculosis* by inhibiting mycobacterial enoyl reductase, InhA. Unfortunately, the efficacy of isoniazid is limited by the development of multidrug-resistant (MDR) isolates. Here, using phenotypic high-throughput whole-cell screening, Manjunatha *et al.* identify a new class of orally-active small-molecule mycobactericidal agents, the 4-hydroxy-2-pyridones, which act by binding to the InhA–NADH complex to occupy the enoyl substrate-binding site. The lead compound, NITD-916, was active against a panel of isoniazid-resistant MDR-TB clinical isolates and demonstrated *in vivo* efficacy in both acute and established mouse TB infection models.

ORIGINAL RESEARCH PAPER Manjunatha, U. *et al.* Direct inhibitors of InhA are active against *Mycobacterium tuberculosis*. *Sci. Transl Med.* **7**, 269ra (2015)

ANTIBODY DESIGN

Hormone–CDR fusions enhance hormone efficacy

Various endocrine hormones are used therapeutically but, owing to short circulating half-lives, they typically must be administered frequently and at high doses. To address this, Liu *et al.* fused human growth hormone (GH) and human leptin as functional domains into the complementarity-determining regions (CDRs) of the humanized therapeutic antibody trastuzumab. The resulting fusion proteins expressed in mammalian cells in good yields and maintained the biological activity of the native hormones. The GH–antibody and leptin–antibody fusions exhibited increased half-lives and notably extended activities in a GH-deficient rat model and a leptin-deficient obese mouse model, respectively.

ORIGINAL RESEARCH PAPER Liu, T. *et al.* Functional human antibody CDR fusions as long-acting therapeutic endocrine agonists. *Proc. Natl Acad. Sci. USA* http://www.pnas.org/cgi/doi/10.1073/pnas.1423668112 (2015)

ENDOMETRIOSIS

Suppressing the oestrogen-inflammatory axis

Current therapies for endometriosis, which focus on reducing systemic oestrogen levels, are limited by side effects and poor efficacy. Zhao *et al.* previously developed two oestrogen receptor (ER) ligands with strong anti-inflammatory activity — chloroindazole (CLI) and oxabicycloheptene sulfonate (OBHS), which target ERα and ERβ, respectively. Here, they show that together, OBHS and CLI prevent the establishment of endometriotic lesions and reverse the growth and progression of established lesions in a mouse model of endometriosis, without affecting reproductive physiology and fertility.

ORIGINAL RESEARCH PAPER Zhao, Y. *et al.* Dual suppression of estrogenic and inflammatory activities for targeting of endometriosis. *Sci. Transl Med.* **7**, 271ra9 (2015)

NATURAL PRODUCTS

Enhancing production

Microorganisms can be metabolically engineered to produce natural metabolites, but it is challenging to functionally express eukaryotic enzymes that are required for compound synthesis while obtaining high-yield production. Here, Zhou *et al.* demonstrate the concept of synthetic microbial consortia, in which one microbe is engineered to synthesize a metabolic intermediate that is translocated to another microbe, where it is further functionalized. For example, in co-culture, *Escherichia coli* was used to rapidly synthesize taxadiene (the scaffold molecule of the anticancer drug paclitaxel), which was then functionalized by *Saccharomyces cerevisiae* to produce high titres of oxygenated taxanes.

ORIGINAL RESEARCH PAPER Zhou, K. *et al.* Distributing a metabolic pathway among a microbial consortium enhances production of natural products. *Nature Biotech.* http://www.nature.com/nbt/journal/vaop/ncurrent/full/nbt.3095.html (2015)