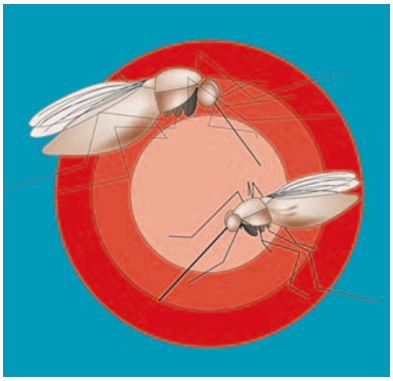
IN BRIEF



MALARIA

Inhibitors of *Plasmodium falciparum* methionine aminopeptidase 1b possess antimalarial activity.

Chen, X. *et al. Proc. Natl Acad. Sci. USA* **103**, 14548–14553 (2006)

New antimalarial drugs are needed to address major limitations of current therapies, particularly drug resistance. Chen and colleagues identified a compound that inhibited the *in vitro* proliferation of chloroquinine-sensitive and multidrug-resistant strains of the malaria-causing parasite *Plasmodium falciparum*. In a mouse model of malaria, the compound was active against chloroquinine-sensitive and -insensitive *P. falciparum* strains. So, inhibitors of PfMetAP have the potential to circumvent resistance to current antimalarial drugs.

ANTIBACTERIAL DRUGS

An alternative bactericidal mechanism of action for lantibiotic peptides that target lipid II.

Hasper, H. E. *et al. Science* **313**, 640–644 (2006)

The rise of antibiotic resistance has highlighted the need to develop new classes of antibiotics. Hasper and colleagues have described a new mechanism by which lantibiotics — polycyclic peptides containing unusual amino acids that have binding specificity for bacterial cells — kill Gram-positive bacteria. The mechanism involves removing lipid II, a key molecule in bacterial peptidoglycan synthesis, from the cell division site, thereby blocking cell-wall synthesis. This mechanism of bactericidal activity does not seem to have any known candidate resistance mechanisms.

CANCER

A2A adenosine receptor protects tumour from antitumour T cells.

Ohta, A. *et al. Proc. Natl Acad. Sci. USA* **103**, 131–137 (2006)

The use of antitumour T cells in cancer therapies is hampered by an unidentified immunosuppressive mechanism of cancerous tissues. Now, Ohta and collegagues have shown that the adenosine A_{2A} receptor ($A_{2A}R$) protects cancerous tissues by inhibiting incoming antitumour T lymphocytes. Genetic deletion of $A_{2A}R$ resulted in rejection of established immunogenic tumours in 60% of host mice. The use of antagonists or small interfering RNA against $A_{2A}R$ improved the inhibition of tumour growth, destruction of metastases and prevention of neovascularization by antitumour T cells. Therefore, $A_{2A}R$ antagonism could enhance immune-mediated tumour destruction.

HIV

Small molecules that bind the inner core of gp41 and inhibit HIV envelope-mediated fusion.

Frey, G. *et al. Proc. Natl Acad. Sci. USA* **103**, 13938–13943 (2006)

HIV enters cells by membrane fusion in a process mediated by the viral envelope protein gp160, which requires cleavage into gp120 and the fusion-promoting fragment gp41 for activation. Frey and colleagues have identified several compounds that prevent the formation of post-fusion gp41. The compounds inhibited envelope-mediated membrane fusion in both cell–cell fusion and viral infectivity assays. When tested against a panel of envelope proteins from primary HIV isolates, the compounds inhibited fusion across a broad range of clades, including macrophage- and T-cell-tropic strains.