IN BRIEF

ANTIVIRAL DRUGS

Dogfish shark chemical has broad-spectrum activity

Zasloff *et al.* showed that squalamine, a compound first isolated from the dogfish shark and known to have antimicrobial properties, also has broad-spectrum antiviral activity against human pathogens. *In vitro* the compound was effective against dengue virus and hepatitis, and *in vivo* it was effective against yellow fever, encephalitis virus and cytomegalovirus. The authors postulated that squalamine, a cationic amphipathic sterol, neutralizes the negative electrostatic surface charge of intracellular membranes so that the cell is less able to support viral replication. Squalamine is readily synthesized and is safe in humans, so it could represent a new antiviral agent.

ORIGINAL RESEARCH PAPER Zasloff, M. *et al.* Squalamine as a broad-spectrum systemic antiviral agent with therapeutic potential. *Proc. Natl Acad. Sci. USA* **108**, 15978–15983 (2011)

G PROTEIN-COUPLED RECEPTORS

Homology model allows effective virtual screening

This study compared virtual screens against a homology model of a G protein-coupled receptor and the experimentally determined crystal structure. Following determination of the crystal structure of the dopamine D3 receptor, but before the information was publicly available, the scientific community was asked to predict the structure of the D3 receptor based on homology models. Remarkably, a docking screen against one such homology model was as effective at prioritizing active D3 ligands — with respect to hit rate, potency and novelty — as a screen against the subsequently released crystal structure.

ORIGINAL RESEARCH PAPER Carlsson, J. *et al.* Ligand discovery from a dopamine D_3 receptor homology model and crystal structure. *Nature Chem. Biol.* 18 Sep 2011 (doi:10.1038/nchembio.662)

CANCER

New avenues for brain tumour therapy

Two papers now suggest potential new lead compounds and adjuvant therapies for the treatment and management of brain tumours. Buckingham *et al.* investigated the aetiology of epileptic seizures caused by the presence of primary brain tumours. Brain slices from a mouse model of tumour-induced seizures exhibited an increase in glutamate release from the tumour, which was mediated by the system x_c^- cysteine–glutamate transporter. Moreover, the resultant epileptic glutamatergic hyperexcitability spread into adjacent brain tissue. Blockade of glutamate release using sulfasalazine — an approved drug that blocks system x_c^- — reduced the frequency of epileptic events in tumour-bearing mice, suggesting that this drug could be used to ameliorate peritumoural seizures. In the second study Atkinson *et al.* used multicell screening, kinome-wide binding assays and a mouse model to identify potential new treatments for the chemoresistant brain tumour ependymoma. They identified kinases within the insulin signalling pathway and the centrosome cycle as regulators of ependymoma cell proliferation, which could be blocked using the corresponding inhibitors. In addition, approved drugs with selective toxicity against ependymoma cells were identified. Moreover, the approach used by the authors could be used to identify leads for other rare cancers.

ORIGINAL RESEARCH PAPERS Buckingham, S. C. *et al.* Glutamate release by primary brain tumors induces epileptic activity. *Nature Med.* 11 Sep 2011 (doi:10.1038/nm.2453) | Atkinson, J. M. *et al.* An integrated *in vitro* and *in vivo* high-throughput screen identifies treatment leads for ependymoma. *Cancer Cell* **20**, 384–399 (2011)