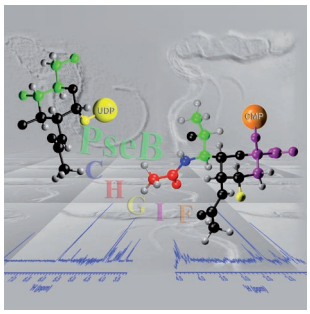
## COVER PICTURE



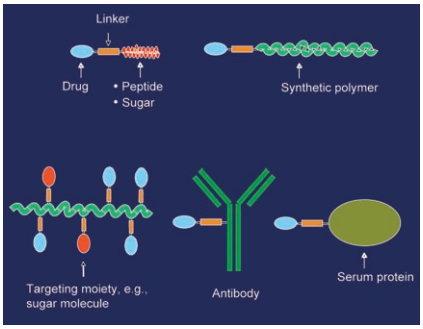

**The cover picture shows** the six enzymes (Pse B, C, H, G, I, F) responsible for producing CMP-pseudaminic acid (CMP-Pse) starting from UDP-GlcNAc in *Campylobacter jejuni* and *Helicobacter pylori*. These pathogens modify their flagella with sialic acid-like sugars such as pseudaminic acid (Pse) which are required for flagellar assembly, motility, and hence virulence. Pse B plays a central role in Pse biosynthesis and is also thought to be implicated in other glycan pathways making it a prime therapeutic target. Saturation transfer difference nuclear magnetic resonance spectroscopy (STD NMR) was used to determine binding epitopes for Pse B and to characterize Pse B inhibition with CMP-Pse at the molecular level. Docking studies and CORCEMA calculations validated STD NMR results and revealed that CMP-Pse and UDP-GlcNAc adopt similar conformations within the Pse B active site. These findings will guide the development of small-molecule inhibitors as a means to pharmaceutically control *C. jejuni* and *H. pylori* infections. For details, see the Communication by D. J. McNally, et al. on p. 55 ff.

## NEWS



## REVIEWS

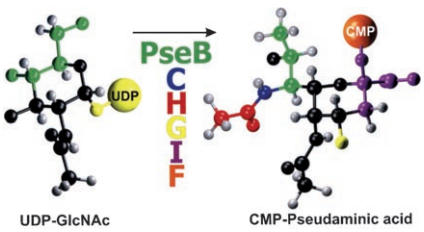





**Targeted delivery**: Many carrier-linked prodrugs have been developed over the past three decades with the goal of improving the therapeutic index of anticancer agents. In this review we elucidate the two main concepts that underlie the design of most anticancer prodrugs: drug targeting and controlled release of the drug at the tumor site.

## COMMUNICATIONS



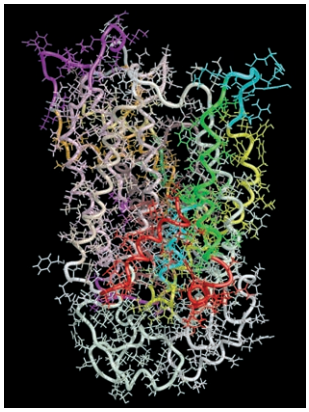



**Deadly decorations**. *Campylobacter jejuni* and *Helicobacter pylori* decorate their flagella, which are essential for virulence, with pseudaminic acid (Pse). Pse production is feedback-regulated in the bacterial cell by CMP-pseudaminic acid, a potent inhibitor of PseB, the first enzyme of the Pse pathway. Herein, STD NMR was used to map binding epitopes for PseB and to characterize the interaction between PseB and CMP-Pse.

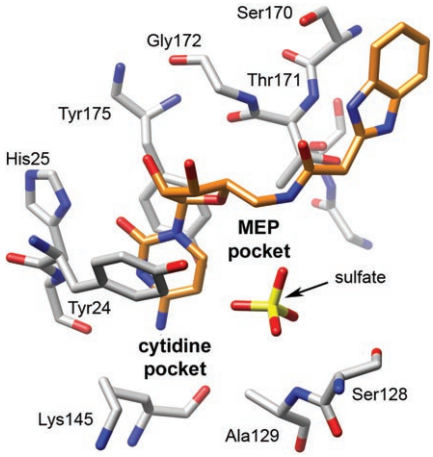
## FULL PAPERS





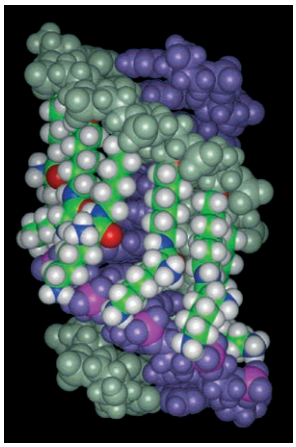
**The glutamate transporters** EAATs are involved in many neurodegenerative diseases. The aim of this study was to generate a model for the human EAAT1 in its homotrimeric structure using a fragmental approach. The model was validated by docking analyses and pharmacophore mapping using a set of 32 known ligands.






**The binding modes** of two water-soluble, cytidine-based inhibitors in complex with the *A. aeolicus* kinase IspE were elucidated by co-crystal structure analysis. Because key active site residues in *A. aeolicus* IspE are identical to those of the corresponding enzymes of *M. tuberculosis* and *P. falciparum*, useful structural information was gained for future structure-based development of inhibitors of the parasite enzymes.

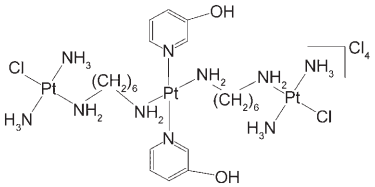




**Cationic nucleotides** consisting of lysine tethered by a 2′-*O*-aminohexyl linker to uridine incorporated into siRNA increase target affinity and can be used in functional oligonucleotides for effective gene silencing in vitro. In DNA-based antisense oligonucleotides, affinity to the RNA complement was decreased, but the in vitro activity increased with a greater number of modifications.

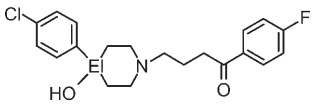
  



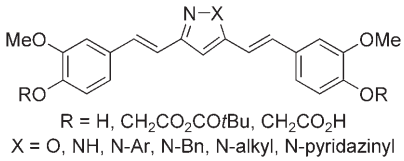
**Anticancerous complexes**. Although highly effective against testicular and ovarian cancers, cisplatin and its analogues have a limited spectrum of activity, numerous side effects, and the problem of intrinsic and/or acquired resistance. This paper describes the synthesis, characterisation, and cytotoxicity of a novel trinuclear platinum complex TH1 (shown) which has the potential to become a highly active anticancer drug.





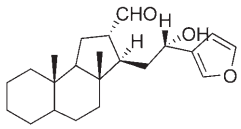

**Sila-haloperidol** (**1 b**), a silicon analogue of the dopamine ($D_2$) antagonist haloperidol (**1 a**), was synthesized. As shown in receptor binding studies, sila-haloperidol (**1 b**) shows a higher potency at $hD_2$ receptors than the parent carbon compound **1 a** and exhibits higher subtype selectivity at dopamine receptors and at σ receptors as well. The metabolic fates of the C/Si analogues **1 a** and **1 b** are totally different.






**Curcumin-derived isoxazoles and pyrazoles** minimize the metal chelation properties of curcumin. Replacement of the 1,3-dicarbonyl moiety with isosteric heterocycles turns curcumin analogue isoxazoles and pyrazoles into potent ligands of fibrillar $A\beta_{42}$ aggregates. Additionally, several compounds are potent inhibitors of tau protein aggregation and depolymerized tau protein aggregates at low micromolar concentrations.





**HIV-1 integrase** mediates the integration of reverse-transcribed viral cDNA into the host genome and presents an attractive target for anti-HIV drug development. We report that hyrtiosal, a natural product from the marine sponge *Hyrtios erectus*, known to be a PTP1B inhibitor, could competitively inhibit HIV-1 integrase binding to the viral DNA by a new inhibitor binding site.

## CONFERENCE REPORTS



Supporting information on the WWW (see article for access details).

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## BOOKS



## SERVICE



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