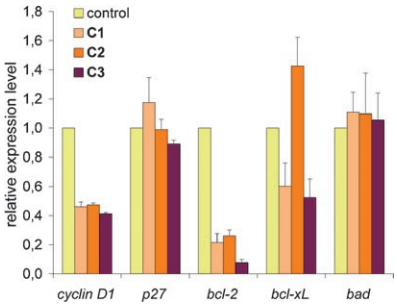
Cell-Cycle Regulation

J. Gao, Y.-G. Liu, Y. Zhou, L. M. Boxer, F. R. Woolley, R. A. Zingaro**

Artificial Zinc(II) Complexes Regulate Cell Cycle and Apoptosis-Related Genes in Tumor Cell Lines

ChemBioChem
DOI: **10.1002/cbic.200600299**



Death metal. Novel luminescent zinc(II) complexes have been found to penetrate through the cell membrane and induce apoptosis in malignant cell lines. The *meso*- species of a set of cyclic zinc(II) complexes (**C3**) was found to be an efficient regulator of the anti-apoptotic gene, *bcl-2* (see figure). This study highlights a new approach to the use of zinc(II)-based complexes as potential drugs.

Enzyme Photochemistry

*P. Rathert, T. Raskó, M. Roth, K. Ś. Kiss, A. Pingoud, A. Kiss, A. Jeltsch**

Reversible Inactivation of the CG Specific SssI DNA (Cytosine-C5)-Methyltransferase with a Photocleavable Protecting Group

ChemBioChem
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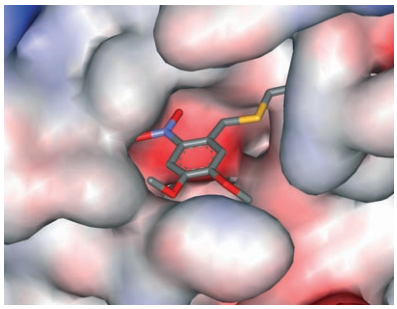
Trick of the light. We describe the covalent modification of the SssI DNA methyltransferase (M.SssI) with 4,5-dimethoxy-2-nitrobenzyl-bromide (DMNBB) to obtain M.SssI with a caged active-site Cys residue (see figure). Irradiation of the caged enzyme with near-ultraviolet light restored its catalytic activity. The results indicate that caging by DMNBB can be used for the reversible inactivation of DNA methyltransferases.

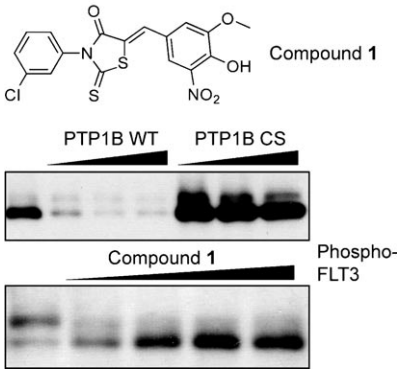


Phosphatase Inhibition

*M. Stuible, L. Zhao, I. Aubry, D. Schmidt-Arras, F.-D. Böhmer, C.-J. Li, M. L. Tremblay**

Cellular Inhibition of Protein Tyrosine Phosphatase 1B by Uncharged Thioxothiazolidinone Derivatives

ChemBioChem
DOI: **10.1002/cbic.200600287**



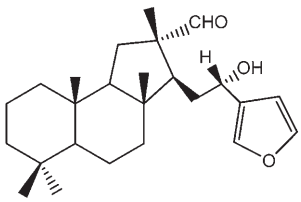
Charge less. We show that a novel inhibitor (**1**) of PTP1B is active in cells at low micromolar concentrations and prevents PTP1B-mediated dephosphorylation of the FLT3-ITD receptor tyrosine kinase (shown). We have synthesized a series of derivatives for basic SAR analysis and have conducted computer-modeling studies to predict its binding mode. This class of uncharged inhibitors could be a starting point for the development of new drugs targeting protein tyrosine phosphatases.

Natural Products

T. Sun, Q. Wang, Z. Yu, Y. Zhang, Y. Guo, K. Chen, X. Shen,* H. Jiang**

Hyrtiosal, a PTP1B Inhibitor from the Marine Sponge *Hyrtios erectus*, Shows Extensive Cellular Effects on PI3K/AKT Activation, Glucose Transport, and TGFβ/Smad2 Signaling

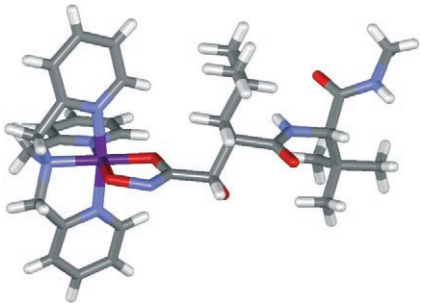
ChemBioChem
DOI: **10.1002/cbic.200600349**



A potential insulin mimetic. Protein tyrosine phosphatase 1B (PTP1B) negatively regulates insulin signaling, and PTP1B inhibitors have been seen as promising therapeutic agents against obesity and type 2 diabetes. Here we report that hyrtiosal, a marine natural product from the marine sponge *Hyrtios erectus* and newly identified as a PTP1B inhibitor, shows extensive cellular effects on PI3K/AKT activation, glucose transport, and TGFβ/Smad2 signaling.

Drug Delivery

Hypoxia-activated cobalt prodrugs: A Co^{III} complex of the matrix metalloproteinase (MMP) inhibitor marimastat (crystal structure shown), designed to selectively deliver the inhibitor to hypoxic tumour sites, exhibits enhanced biological activity in a mouse model.

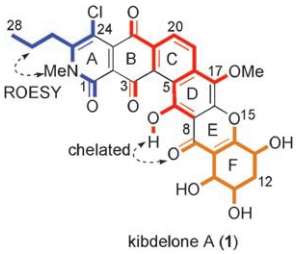


*T. W. Failes, C. Cullinane, C. I. Diakos, N. Yamamoto, J. G. Lyons, T. W. Hambley**

Studies of a Cobalt(III) Complex of the MMP Inhibitor Marimastat: A Potential Hypoxia-Activated Prodrug

Chem. Eur. J.
DOI: **10.1002/chem.200601137**

Natural Products



kibdelone A (**1**)

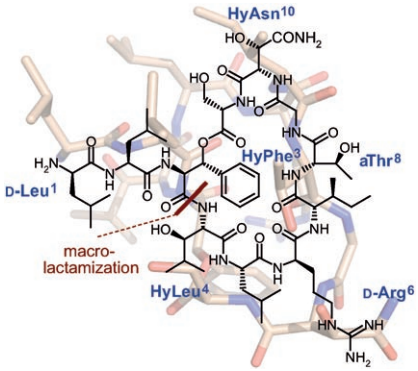
A rare *Kibdelosporangium* sp. isolated from an Australian soil sample has been found to produce the kibdelones (see figure), a novel family of heterocyclic polyketides that exhibit potent and selective cytotoxicity against a panel of human tumor cell lines, and also display significant antibacterial and nematocidal properties.

*R. Ratnayake, E. Lacey, S. Tennant, J. H. Gill, R. J. Capon**

Kibdelones: Novel Anticancer Polyketides from a Rare Australian Actinomycete

Chem. Eur. J.
DOI: **10.1002/chem.200601236**

Antibiotic Resistance



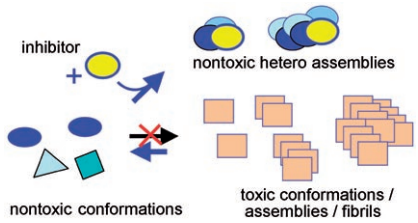
Tackle-resistant bacteria: Determination of the 3D structure of the antibiotic lysobactin has led to its total synthesis and resulted in a high-yielding macrolactamization step. The minimal use of protecting groups allowed preorganization of the side chains to steer the cyclization. Thus, a new chemical route has been developed in the search for innovative antibiotic lead structures.

F. von Nussbaum, S. Anlauf, J. Benet-Buchholz, D. Häbich, J. Köbberling, L. Musza, J. Telser, H. Rübsamen-Waigmann, N. A. Brunner*

Structure and Total Synthesis of Lysobactin (Katanosin B)

Angew. Chem. Int. Ed.
DOI: **10.1002/anie.200604232**

Protein Aggregation



Le fabuleux destin d'amyloid disease: A peptide-derived inhibitor for amyloid diseases binds the Alzheimer's disease β-amyloid peptide (Aβ40) and the type II diabetes islet amyloid polypeptide (IAPP) and blocks cytotoxic self-assembly of both peptides. Evidence is also presented for a high-affinity interaction between Aβ40 and IAPP that results in cross-suppression of cytotoxic self-association of both peptides.

*L.-M. Yan, A. Velkova, M. Tatarek-Nossol, E. Andreetto, A. Kapurniotu**

IAPP Mimic Blocks Aβ Cytotoxic Self-Assembly: Cross-Suppression of Amyloid Toxicity of Aβ and IAPP Suggests a Molecular Link between Alzheimer's Disease and Type 2 Diabetes

Angew. Chem. Int. Ed.
DOI: **10.1002/anie.200604056**

