

## Poster Sessions

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**Keywords:** metal-organic polymer, scandium, supramolecular

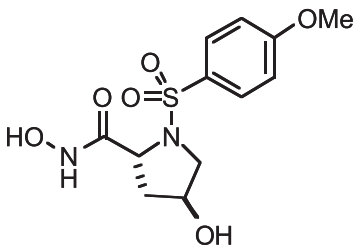
### MS31.P25

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#### Inhibition of MMP-1, 3, and 13 by Same Inhibitor – Structure Based Design Study

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Matrix metalloproteinase (MMP) inhibitors are potential therapeutic agents for various diseases including cancer and osteoarthritis. Recent data from clinical trials with MMP inhibitors indicate that there is a great need for selective inhibitors. X-ray crystallography [1], [2], [3] has been used as a tool to help understand specific binding interactions of inhibitors to various MMPs. Large conformational changes have been noted when comparing the structures of the active MMP-3 catalytic domain and the one inhibited by a hydroxamic acid inhibitor. Both soaking and co-crystallization methods were used to generate the MMP-3/ inhibitor complex crystals for data collection. The same inhibitor has also been co-crystallized with MMP-1 and MMP-13. Comparisons of the structures of three inhibited enzymes, MMP-1, 3, and 13 show that MMP-3 and 13 are extremely similar. There are major differences in the binding pockets, especially in the S1' pocket between MMP-1 and MMP-3/13. These structural studies have helped design more selective inhibitors that can be used as therapeutic agents with improved safety profile.



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**Keywords:** osteoarthritis, drug, design

### MS31.P26

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#### Understanding the Phases of DNAN

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Dinitroanisole (DNAN) is a key insensitive munition melt-phase ingredient that is currently featured in several melt-pour formulations developed by the U.S. Army. Current interest in DNAN has arisen due primarily to its ability to provide a less sensitive melt-cast medium than TNT, allowing for the development of less sensitive melt-cast formulations.

It is known in the literature that crystalline DNAN exists in two

phases, A and B, that melt at 96(1)°C and 87(1)°C respectively. During this study, a third phase (C) was observed during a variable temperature study of the low melting point sample. It has also been observed that a spontaneous phase transition of B to A occurs under ambient conditions. Each phase has been isolated and detailed crystallographic studies of the three phases have been done, as well as some theoretical energy calculations. The transition from B to C is reversible and straightforward due to the ordering of a disordered nitro group at low temperature. The transition from B to A is far more complex, requiring a large molecular rotation of DNAN molecules.

**Keywords:** phase transition

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#### Regioselective deacetylation based on teicoplanin-complexed Orf2\* crystal structure

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Lipoglycopeptide antibiotics are more effective than vancomycin against MRSA as they carry an extra aliphatic acyl side chain on glucosamine (Glm) at residue 4 (r4)[1]. The biosynthesis of the r4 N-acyl Glc moiety at teicoplanin (Tei) or A40926 has been elucidated, in which the primary amine nucleophile of Glm is freed from the r4 GlcNac pseudo-Tei precursor by Orf2\* for the subsequent acylation reaction to occur[2]. In this report, two Orf2\* structures in complex with -D-octyl glucoside or Tei were solved. Of the complexed structures, the substrate binding site and a previously unknown hydrophobic cavity were revealed, wherein r4 GlcNac acts as the key signature for molecular recognition and the cavity allows substrates carrying longer acyl side chains in addition to the acetyl group. On the basis of the complexed structures, a triple-mutation mutant S98A/V121A/F193Y is able to regioselectively deacetylate r6 GlcNac pseudo-Tei instead of that at r4. Thereby, novel analogs can be made at the r6 sugar moiety.

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**Keywords:** regioselective, glycopeptide antibiotic, deacetylase.

### MS31.P28

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#### Crystal structure of T-H protein complex of the glycine cleavage system

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Aminomethyltransferase, a component of the glycine cleavage system termed T-protein, reversibly catalyzes the degradation of the aminomethyl moiety of glycine attached to the lipoate cofactor of H-protein, resulting in the production of ammonia, 5,10-methylenetetrahydrofolate, and dihydrolipoate-bearing H-protein in the presence of tetrahydrofolate (THF). Several mutations in the human T-protein gene are known to cause non-ketotic hyperglycinemia. Previously we determined the