

(DESY) control system, MxCuBE (ESRF) and EDNA (www.edna-site.org).

Keywords: Synchrotron beamlines, instrumentation, microcrystals

FA1-MS01-P06

Structural biology of the nogalamycine biosynthetic pathway. Magnus Claesson, Gunter Schneider. *Mol. Struct. Biol., Karolinska Institutet, Sweden*.
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Anthracyclines are polyketide antibiotics with a high cytostatic potency and are used in the treatment of a wide range of tumor types. The usage is however limited by a cumulative cardiotoxicity, giving rise to severe side effects during and after treatment. There is therefore a need for new polyketide antibiotics, with reduced toxicity and maintained therapeutic effect.

As part of an on-going effort in the laboratory to characterize the biosynthetic pathways of anthracyclines, five genes encoding glycosyltransferases from two *Streptomyces* species have been cloned. One of these was successfully produced in soluble form and purified to homogeneity. Crystallization screening yielded crystals at several conditions and one of these conditions was scaled up, providing one data quality crystal from which data was collected. Crystal reproduction was optimized, however due to size limitations of the crystals no additional data quality crystals could be obtained. Reductive methylation was successfully utilized to improve crystal quality and reproducibility. Methylation appears not to have given rise to any new crystal contacts or changes in crystal packing, and the crystals were obtained in roughly the same conditions. The beneficial, but rather elusive, effect of the methylation seems to be a reduction in protein diversity, where the chemical treatment causes instable protein to aggregate. Furthermore the remaining protein is less likely to aggregate over time and seems less prone to excessive nucleation as compared with the native protein. The structure of this glycosyltransferase has been determined to 2.7 Å in complex with a ligand, using molecular replacement.

Keywords: glycosyltransferases, natural products, X-ray macromolecular structure

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Facilities for Structural Biology and Chemical Crystallography at Diamond. Michael Engel, Elizabeth J. Shotton. *Diamond Light Source Ltd, Harwell Science & Innovation Campus, Didcot, Oxfordshire, OX11 0DE, UK*.
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Diamond Light Source was opened in October 2007. Phase I construction comprised the building, the machine and the first seven experimental stations. As part of Phase I, three macromolecular crystallography beamlines I02, I03 and I04 were built. The three beamlines will be tunable over the wavelength range 0.5 - 2.5 Å, to enable MAD experiments to be carried out with all three beamlines optimised for performance around the Se K-edge. Robotic systems for automated sample handling and crystal centring, and software

allowing automated data collection have led to highly efficient and productive beamlines.

Facilities for remote monitoring and beamline operation further enhance the performance, and the implementation of biological containment at category 3 level on beamline I03 will allow pathogens to be studied.

I24, the tunable microfocus macromolecular crystallography beamline, became operational in July 2008 as part of Phase II. With a beamsize of 5-30 microns it enables measurements on small crystals that are not possible on conventional beamlines, due to their small size or mosaicity. With its ability to mount SBS-format plates it also improves the screening of crystals for optimisation of crystallisation conditions.

Two beamlines for structural chemistry have also opened recently. I11 provides high resolution, high throughput powder diffraction and I19 is a small molecule crystallography beamline suitable for studying microcrystals and weakly diffracting samples as well as excited state systems.

Further crystallography beamlines include a fixed wavelength MX station (I04.1) for high throughput experiments (currently under commissioning with 25% user mode) and I23, a long wavelength MX beamline (currently in the design phase).

Keywords: structural chemistry and biology, X-ray crystallography, synchrotron X-ray diffraction

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Sulfolobus solfataricus Adenine Phosphoribosyltransferase. Sune F. Husted^a, Kristine S. Jensen^b, Anne Mølgaard^a, Jens-Christian N. Poulsen^b, Anders Kadziola^a, Kaj Frank Jensen^b. *^aDepartment of Chemistry and ^bDepartment of Biology, University of Copenhagen, Denmark*.
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Phosphoribosyltransferases (PRTases) are a group of enzymes that catalyze the formation of nucleotide 5'-monophosphates as essential precursors in the synthesis DNA or RNA. They all use a common substrate, 5-phosphoribosyl- α -1-pyrophosphate (PRPP), and transfer nucleobases to C1 of the ribose 5'-phosphate moiety of PRPP to form nucleotide 5'-monophosphates under the release pyrophosphate ($P_2O_7^{4-}$). PRTases are involved in both the *de novo* biosynthesis of nucleotides, e.g. orotate PRTase (OPRTase) and in the salvage path-ways, e.g. uracil PRTase (UPRTase), adenine PRTase (APRTase) and hypoxanthine-guanine-xanthine PRTases (HGXPRTases; often with mixed specificity). PRTases share a common domain fold (type 1) which defines the specificity for PRPP and a variable domain for recognition of the various nucleobases.

Adenine PRTase structures are known for eukaryotes and bacteria and details of their active sites have been mapped out. APRTase from the thermophile archaean *Sulfolobus solfataricus* is an enzyme with unexpected properties: The substrate binding order is reversed with adenine binding first followed by PRPP. It has a double pH optimum and is potently inhibited by AMP and ADP. Sequentially it does not resemble other APRTases but merely HGXPRTases from eukaryotes, bacteria and archaea. The closest sequence homologues in PDB used for molecular replacement share about 31 % sequence identity for a 143/210 residue stretch of the sequence. The remaining sequence does not resemble any known structure. *Ss*APRTase is to our knowledge the first archaean APRTase to be structurally characterized.