not resemble any known structure. *Ss*APRTase is to our knowledge the first archaean APRTase to be structurally characterized.

We will present dimeric $P6_1$ structures of "apo" *Ss*APRTase (with PO_4^{3-}) together with the complexes *Ss*APRTase:AMP (product) and *Ss*APRTase:ADP (inhibitor) based on ESRF (Grenoble) synchrotron data to about 2.4 Å resolution. The current work concentrates on obtaining substrate complexes of *Ss*APRTase.

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UDP-Sugar derivatives reveal novel dynamic features of blood group glycosyltransferases

Rene Jørgensen,[a] Thomas Pesnot,[b] Gerd K. Wagner,[b] Monica Palcic,[a] *[a]Carlsberg Laboratory, Gamle Carlsberg Vej 10, 2500 Valby, Copenhagen, (Denmark) [b]King's College London, School of Biomedical Sciences, Inst. of Pharmaceutical Science, 150 Stamford Street, London SE1 9NH, (England).* E-mail: Rene.Jorgensen@Carlsberglab.com

Glycosyltransferases (GTs) are carbohydrate-active enzymes with essential roles in numerous fundamental biological processes such as cellular adhesion, cell signaling, carcinogenesis and cell wall biosynthesis in human pathogens. These enzymes therefore underpin human health and disease and thus inhibitors of GTs are highly sought after as small molecular tools for chemical biology and as lead compounds for drug discovery. Previously, reported ground-state GT donor or acceptor analogues often possess only limited inhibitory potency and the design is complicated by the complex reaction mechanism.

Recently, new and potent GT inhibitors were developed by structural modification of the UDP-galactose donor at position 5 of the uracil base (figure 1) [1]. Initially, we solved the crystal structure of a representative GT with the most potent UDP-sugar derivative bound. The complex structure reveals that the derivative binds in the active site in a similar manner as the natural donor, but almost completely abolishes sugar transfer by locking the target enzyme in a catalytically inactive conformation [2]. This unique mode of inhibition for GTs seems to be generally applicable to other enzymes in this family. Interestingly, new structures of other similar UDP-sugar derived inhibitors bound to the active site including binding of acceptor reveal striking adaptive dynamics of the enzyme and provide an explanation for its ability to remain slightly active. In addition, the new structures provide an explanation for the dependence of inhibitory potency on the subsituent structure. Finally, by modifying a UDP-GalNAc we have for the first time obtained a structure with an intact UDP-GalNAc in the binding site of human blood group GTs. This structure reveals important aspects of the specificity of the enzymes responsible for creating blood type A and B. These results demonstrate the dynamics of the GTs and provide a template for the development of a new class of allosteric GT inhibitors.

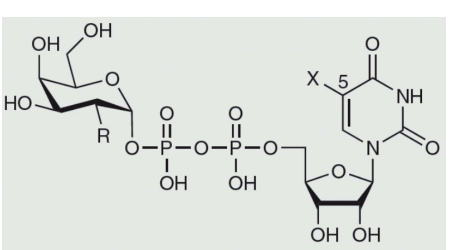

Figure 1

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The 1.3 Å structure of copper nitrite reductase from thermophilic denitrifer

Yohta Fukuda,[a,b,c] Taro Tamada,[c] Hideto Takami,[d] Tsuyoshi Inoue[b] and Masaki Nojiri,[a] *[a]Dept. of Chem., Grad. School of Sci., Osaka Univ. (Japan). [b]Dept. of Mat. Chem., Grad. School of Eng., Osaka Univ. (Japan). [c]Mol. Biol. Reseach Center, Quantum Beam Sci. Directorate, JAEA (Japan). [d]Microb. Genome Reseach Group, JAMSTEC (Japan).* E-mail: y_fukuda@chem.eng.osaka-u.ac.jp

Denitrification is known as anaerobic respiration in which nitrogenous compounds (NO_2^- or NO_3^-) are used as terminal electron acceptors. Copper-containing nitrite reductase (CuNIR) catalyzes the one electron reduction of nitrite to nitric oxide (NO), which is the key step in the denitrification pathway. This enzyme folds a homo-trimeric structure, having two copper binding sites per a monomeric unit. The type 1 copper (T1Cu) relays an electron from the electron-donor to the type 2 copper site (T2Cu). The T2Cu is located at the interface of adjacent monomers and coordinated by a water molecule and three histidine residues, serving as the active site for nitrite reduction. Though a wide variety of microorganisms is involved in denitrification, little attention has been paid to denitrifying extremophiles. The genome of thermophilic *Geobacillus kaustophilus* HTA426 contains denitrification genes including *nirK* encoding CuNIR (*Gk*NIR). The sequence alignment analysis indicated *Gk*NIR shares low sequence identity with other typical CuNIRs. It is essential for understanding the structure-function relationship of the thermophilic CuNIRs in depth to determine the structure of *Gk*NIR. Recently, we have achieved crystallization of *Gk*NIR and performed the preliminary X-ray diffraction analysis [1]. Here, we describe structure analysis of *Gk*NIR at 1.3 Å resolution.

There are main characteristics of *Gk*NIR in two loops (tower loop [2] and extra loop regions) and the N-terminal region. In *Gk*NIR the seventeen-residue deletion in the tower loop results in the shortest tower loop in all the CuNIR structures already solved. An extra loop composed of eleven residues of the downstream of the tower loop is unique to *Gk*NIR. In all the known CuNIRs, a surface Glu forms a hydrogen bond with His ligand for T1Cu and this hydrogen bond provides direct surface accessibility to the T1Cu. However, in *Gk*NIR His95 for T1Cu forms a hydrogen bond with Asp89 positioned on the random coil containing His95. Moreover, Asp89 forms a hydrogen bond with His21 on the N-terminal α-helix. The N-terminal α-helix is positioned in the vicinity of the tower loop. In the known CuNIRs, the tower loop is located near the T1Cu site and constructs the docking surface for the electron donor, cytochrome c_{551} [3]. Superposition of the crystal structure of *Gk*NIR to the known crystal structure of the electron-transfer complex for CuNIR with its electron donor cytochrome c_{551} suggests that the N-terminal α-helix structure may be involved in the protein-protein interaction during formation of electron transfer complex. These characteristic structures found in 1.3 Å *Gk*NIR structure suggest evolutionary diversity of CuNIR and play a key role in functioning in the particular environment where *G. kaustophilus* inhabits.

Figure. Structure of a monomeric unit of *Gk*NIR. The α-helix surrounded by dashed line is the unique N-terminal α-helix and two copper ions are showed as black spheres.