

Structural Studies of B12-Dependent Ribonucleotide Reductase: Another Piece of the Puzzle

M Sintchak, C Drennan, (Mass. Institute of Technology), G Arjara, C Lawrence(Harvard U.), L Shu, B Kellog, J Stubbe

Abstract No. Sint6282

Beamline(s): X25

Abstract: Ribonucleotide reductases (RNRs) catalyze the conversion of nucleotides to deoxynucleotides. Their key role in DNA biosynthesis and repair makes them attractive targets for anti-tumor, anti-viral, and anti-bacterial therapies. Despite their central metabolic functions, ribonucleotide reductases have not been evolutionarily conserved, consisting of very different amino acid sequences and utilizing different metallocofactors to accomplish the same chemistry. We have determined the X-ray crystal structure of coenzyme B12-dependent ribonucleoside triphosphate reductase (RTPR) from *Lactobacillus leichmannii* in the apo enzyme form and in complex with adeninylpentylcobalamin at 1.75 and 2.0 Å resolution, respectively. The native datasets in each case were collected at NSLS Beamline X25. This is the first structure of a Class II RNR, i.e., one that utilizes coenzyme B12 as a cofactor. In some ways, the structure is even more amazing than anticipated. For example, the structure of B12-dependent RTPR is much more similar to other RNR structures than it is to any B12-dependent enzymes. In other ways, these results are puzzling when one contemplates how RTPR may have evolved to utilize a different metallocofactor from the other classes of RNR. This new high resolution structural information will help provide insight into the mechanism and evolution of these essential enzymes.

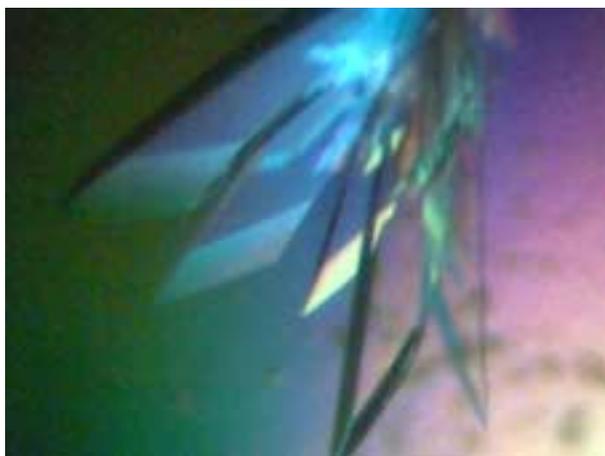


Figure 1: Crystals of apo RTPR

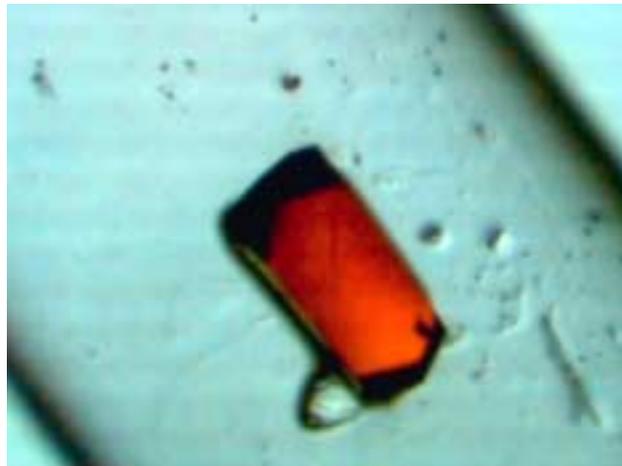


Figure 2: Co-crystals of RTPR with Adeninylnpentylcobalamin