X-ray Crystallographic Study of Thymidylate Synthases from *Corynebacterium glutamicum* NCHU 87078

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TOPIC I. X-ray crystallographic study of thymidylate synthases from Corynebacterium glutamicum NCHU 87078

The genome of Corynebacterium glutamicum NCHU 87078 contains two putative thymidylate synthase genes, designated as CgthyX and CgthyA. ThyX and ThyA are known to catalyze the transfer of a methyl group from CH2H4folate to dUMP and form dTMP. Although they perform the same reactions but their catalytic mechanisms are different. Notably, CgThyX is FAD-dependent thymidylate synthase. In this study, we have determined crystal structures of apo-form and FAD-form CgThyX and apo-form CgThyA. The overall CgThyX structure consists of three domains: the top helical domain, bottom helical domain and a central α/β domain. The CgThyX-FAD structure demonstrated a loose tetramer related by the crystallographic 222 symmetry, in which FAD is chelated between the subunits via a manner distinct from that of other flavin-dependent thymidylate synthases. The CgThyA structure is composed of 7α-helices and 8β-strands organized into three layers. The largest element is six-stranded mixed β-sheet. Structural analysis highlights unique features of the inactive C. glutamicum ThyX that distinguish this enzyme from ThyX proteins of other organisms. On the other hand, the conserved active-site framework is present in CgThyA. Our results together suggest the presence of an atypical thymidylate synthetase ThyX in C. glutamicum requires.

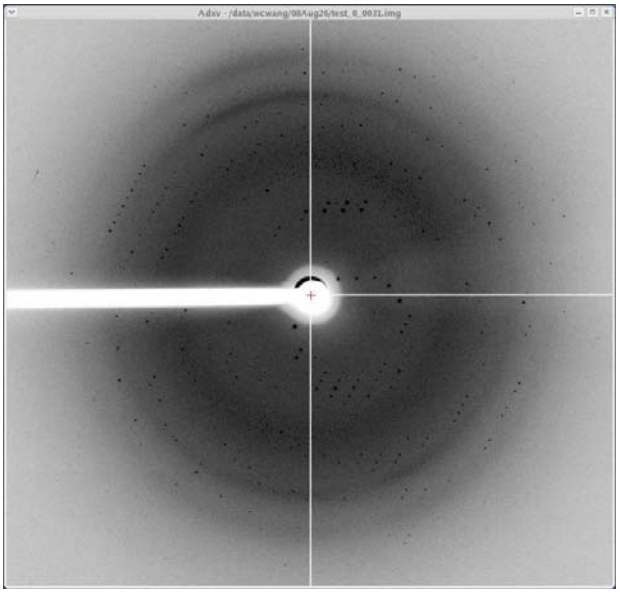

Fig. 1: diffraction pattern of apo-form ThyX at 90°.

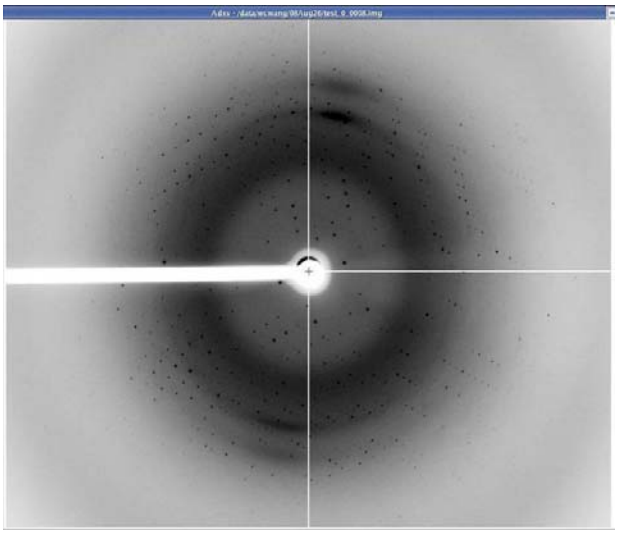

Fig. 2: diffraction pattern of complex form ThyX at 0°.