

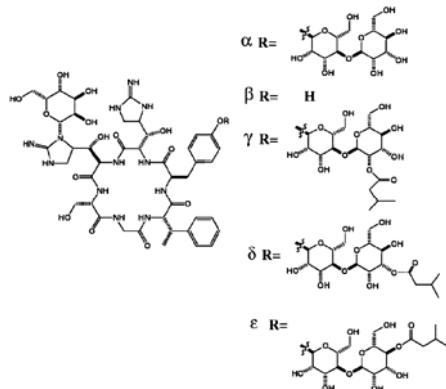
Crystal Structure of MppR in the Biosynthesis of Antibiotic Mannopeptimycin

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Little is known about the formation of the rare D- and L-End residues other than their originate from L-Arg¹. The mannopeptimycins, isolated from a strain of *S. hygrosopicus*, contain D- and L-β-hydroxyenduracididine residues, are the only glycopeptide antibiotics we are aware of that contain this unusual amino acid². Both the mannopeptimycin and enduracidin clusters contain a three-gene operon, mppPQR and endPQR, respectively, which share very high identity. MppPQ are proposed as the PLP-dependent aminotransferases, and the hypothetical protein, MppR, might be involved in the biosynthesis of nonproteinogenic amino acid (2S,3S) β-Hydroxyenduracididine for glycopeptide antibiotic mannopeptimycin (Fig.1).

a)



b)

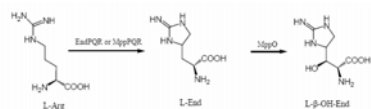


Figure 1. A) The structure of the Manno-peptimycin and the red circle is represent for β-hydroxyenduracididine. B) The proposed mppPQR may be catalyzes the biosynthesis of β-hydroxyenduracididine from L-Arginine .

To realize the mechanism of synthesis pathway, we focus on the MppR protein, which is proposed to be a hypothetical protein which involved in the biosynthesis of mannopeptimycin² in our preliminary studies. The MppR cstrals are obtained using the hanging-drop vapour-diffusion method (Fig.2). There is one molecule per asymmetric unit. The three-dimensional structure (Fig.3) of mppR is subsequently determined by Se-MAD method at NSRRC BL13B1 beamline and the native form is solved by molecular replacement method (Table.1). Further studies are still in progress.

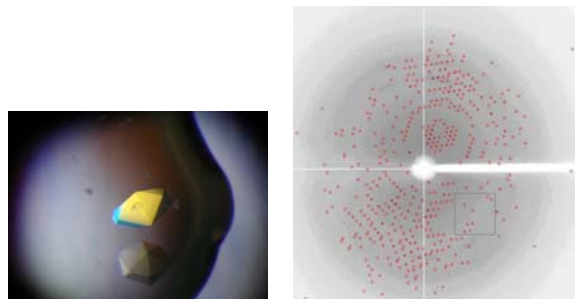


Figure 2. A) The crystal was grown in one week at 20°C. B) The diffraction pattern of the Se-mppR, and the data collection parameter are the Oscillation angle is 0.5°, the expose time is 1 min, and distance of the crystal and detector is about 250mm.

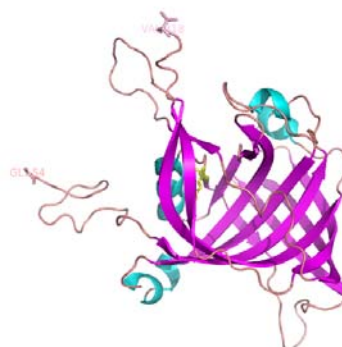


Figure 3. A ribbon diagram of initial mppR structure. The α-helices are colored in blue, and the β-strands are colored in pink.

Native (MppR) Crystal				SeMppR Crystal			
Data collection							
Space group	P6 ₂ 22			P6 ₂ 22			
Cell dimensions							
<i>a</i> , <i>b</i> , <i>c</i> (Å)	160.967	160.967	85.101	161.235	161.235	85.764	
α , β , γ (°)	90.00	90.00	120.00	90.00	90.00	120.00	
				<i>Peak</i>	<i>Inflection</i>	<i>Remote</i>	
Wavelength	0.9			0.9819	0.9820	0.9667	
Resolution (Å)	2.46			2.4	2.4	2.4	
<i>R</i> _{eqn} or <i>R</i> _{map}	0.076			0.096	0.094	0.092	
<i>I</i> / <i>σ</i>	41.94			29.2	17.18	17.8	
Completeness (%)	95.6			99.4	98.0	97.5	
Redundancy	22			19.2	6.4	6.4	

Table 1. Data collection statistics of native and Se-mppR

Reference

1. Agric Biol Chem **48**, 1503–1508 (1984).
2. Chem.Biol **9**, 1175–1187 (2002).