The enzyme EryM gives a helping hand in natural product biosynthesis

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Polyketide synthases (PKS) and non-ribosomal peptide synthetases (NRPS) are essential enzymes responsible for the assembly of natural products, such as the common antibiotic erythromycin and the siderophore erythrochelin. Most bacterial PKS and NRPS biosynthetic pathways are encoded by gene located in a cluster. Interestingly, the enzyme EryM, encoded by a gene apart from any PKS or NRPS gene cluster, was identified to be crucial to producing erythrochelin and erythromycin.1EryM was first identified as a malonyl-CoA decarboxylase.3 Later studies led to the proposal that EryM is an acetyltransferase where the decarboxylation product, acetyl-CoA, is the acetyl group donor.4 The NRPS gene cluster for the erythrochelin pathway lacks an acetyltransferase to generate acetyl-hydroxyl-ornithine as the starter unit, thus EryM provides the missing link. Yet another study demonstrated that eryM is essential for erythromycin biosynthesis. The erythromycin PKS gene cluster lacks any gene for an enzyme to generate the starter unit, propionyl-CoA. Thus, EryM is proposed to form this starter unit by decarboxylation of methylmalonyl-CoA. However, it is still unknown how or whether EryM performs both malonyl- and methylmalonyl-CoA decarboxylation as well as acetyl transfer.

We used structural and biochemical techniques to probe the biological function of EryM. We found that EryM is composed of an N-terminal uncharacterized domain and a C-terminal domain containing the acetyltransferase active site. Purified EryM catalyzed decarboxylation of malonyl-CoA and subsequently used the intermediate acetyl-CoA as a substrate for acetyl transfer. These results suggest that EryM is a bifunctional enzyme that synthesizes the substrate for downstream natural product biosynthesis.