Structural investigation of AlsA, a radical S-adenosylmethionine enzyme involved in the biosynthesis of the oxetane-containing herbicide Albucidin

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Herbicides are a class of molecules commonly employed to maintain high crop yields by targeting weeds, the most damaging class of pests in agriculture [1]. Albucidin is a novel herbicide found in Streptomyces albus subsp. Chlorinus NRRL B-24108 which shows a suspected new mode of action [2]. Albucidin is a nucleoside analogue containing an oxetane moiety similar to the antiviral compound Oxetanocin-A (OXT-A). OXT-A is the only other known naturally occurring oxetane-containing nucleoside analogue and has a biosynthetic pathway with two key enzymes: OxsA and OxsB [3, 4]. OsxB, a B₁₂-dependent Radical S-adenosylmethionine (RS) enzyme, forms the oxetane ring through a ring contraction mechanism [4]. Similarly, the B₁₂-dependent RS enzyme AlsB is predicted to form the oxetane ring in the biosynthetic pathway of Albucidin [5, 6]. However, these biosynthetic pathways diverge after this step. OXT-A is formed through a reduction of the aldehyde by a nonspecific reductase followed by the removal of phosphate(s) through hydrolysis by OsxA while Albucidin is proposed to be formed from the removal of the aldehyde group on the oxetane ring by AlsA, a Biotin synthase (BioB)-like RS enzyme [5, 6]. Although AlsA is most closely related to BioB-like enzymes, with high sequence similarity in the canonical TIM barrel domain, AlsA contains an N-terminal domain of about 100 amino acids which shares minimal sequence homology to RS enzymes with known structures. Here, I provide a progress report on the structural analysis of AlsA using X-ray crystallography.