

## Poster Presentation

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### *Structure-function studies of CrmK, an oxidase involved in Caerulomycin A biosynthesis*

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Caerulomycin A (CRM A) is an immunosuppressive agent that has a unique 2,2'-bipyridine core structure. Isolated from a marine-derived *Actinoalloteichus cyanogriseus*, this natural product exhibits antifungal, anti-amoebic, antitumor, and antimicrobial activities. Its biosynthetic pathway consists of more than 20 enzymes, at least seven of which are putatively involved in post-PKS/NRPS modifications of the scaffold. Among these, CrmK is a flavin-dependent oxidase. We have determined the crystal structure of CrmK bound to its flavin adenin dinucleotide (FAD) cofactor at 1.9 Å resolution. FAD linkage to CrmK is observed via two covalent bonds with protein residues His64 and Cys124. This crystal structure, combined with the activity analysis of both wild-type CrmK and a series of mutants, has revealed the role of active site residues lining the substrate and FAD binding pocket. Our studies add additional molecular insights into the structure and function relationship of the bicovalently flavinylated oxidases.

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