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Elucidate the biosynthesis of nucleoside moiety in albomycin

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Albomycins are broad-spectrum antibiotics isolated from soil-dwelling actinomycetes. The albomycins have a minimum inhibitory concentration (MIC) as low as 10 ng/mL against Streptococcus pneumonia. Studies revealed that albomycins are Trojan horse antibiotics that consist of a siderphore component that is indiscriminately taken up by bacteria as an iron source. Once inside the cell, the albomycins are hydrolyzed to release a nucleoside compound SB-217452, which works as an enzyme inhibitor of bacterial seryl-tRNA synthetase, which is structurally different from other nucleoside antibiotics such as A-90289, caprazamycin and muraymycin. The nucleoside moiety of albomycin has two features: The stereo configuration of 5'-C-glycyluridine (GlyU) in albomycin is (5'R, 6'S), which is different from (5'S, 6'S) in the other nucleoside antibiotics; a sulfur atom replacing the oxygen atom on the pentose ring in albomycin. Gene cluster analyzing indicated that AbmH, a homologue of LipK, is responsible for the incorporation of glycine moiety to the uridine aldehyde. LipK was functionally characterized as a L-threonine: Uridine-5'-aldehyde transaldolase, which catalyzes the C-C bond-forming during the biosynthesis of the GlyU in A-90289. Further characterization of AbmH in *vitro* found that it is covalently bonded to a pyridoxal-5'-phosphate as a cofactor. AbmH has catalyzed an aldo-type reaction to incorporate the glycine moiety on L-threonine to uridine aldehyde to form the GlyU. The product GlyU was confirmed to have (5'R, 6'S) stereo configuration, same as the structure in albomycin. Different substrates test showed that L-allo-threonine could also be used as a substrate in reaction.

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