

The synthesis of fatty acids for cell membrane generation and maintenance is catalysed by fatty acid synthase (FAS). FAS consists of a series of enzymatic activities, either gathered on very large multifunctional polypeptides (type I) or organized from discrete enzymes (type II). Type I systems are found in animal and fungi cytosol, while the presence of Type II systems characterize bacteria and plant plastids. However, it has recently been shown that FAS II proteins are also encoded by nuclear DNA in animals and fungi. In these organisms, the FAS II proteins contain mitochondrial targeting sequences [1]. FAS enzymes are essential for lipid and fatty acid synthesis and are attractive targets for therapeutics. β -Ketoacyl-acyl carrier protein synthase (KAS) is the FAS enzyme catalysing the biosynthetic Claisen condensation reaction. The substrate and product profiles for mitochondrial KAS (mtKAS) from *Arabidopsis thaliana* are different from those characterizing the bacterial enzymes [2].

The crystal structure of the *Arabidopsis thaliana* mtKAS has been determined to 2.0 Å resolution. It is the first structure of a mtKAS. The structure reveals a dimeric enzyme with an $\alpha\beta\alpha\beta$ -fold and a somewhat extended cap region. In contrast to other KAS enzymes, mtKAS can utilize the decarboxylation product of malonyl-ACP in a productive way in the absence of acyl-ACP substrates and can catalyse the condensation of the complete range of saturated acyl-ACP substrates (C_3 - C_{16}) with malonyl-ACP as the only substrate. The role of the active site architecture and possible mtKAS:ACP interactions are discussed and correlated with proposed catalytic mechanisms.

[1] Zhang et al. (2003). J. Biol. Chem. 278, 40067-40074.

[2] Yasuno et al. (2003). J. Biol. Chem. 279, 8242-8251.