Poster

Understanding ladderane biosynthesis: Towards structural and mechanistic insights from an anammox β-ketoacyl-ACP-synthase II

P. Granatino[1], A. Dietl[2], T. Barends[1]

[1]Max Planck Institute for Medical Research, Janhstrasse 29, 69120 Heidelberg (DE), [2]University of Basel, Dept. of Pharmaceutical Sciences, Klingelbergstrasse 50, 4056 Basel (SW)

paola.granatino@mr.mpg.de

[5] and [3]- Ladderanes – unusual fatty acids and alcohols found in lipids of bacteria in the anammox group [1] – have respectively five and three four-membered rings fused to one another, making them sterically very strained [2]. How enzymes overcome the energetic barrier to produce molecules with such unfavourable thermodynamics (high final energy content) is poorly understood.

Through structural and mechanistic studies on an anammox β-ketoacyl-ACP-synthase II [3] we seek to take a step on unrevealing the mechanism behind ladderane biosynthesis.

Anammox β-ketoacyl-ACP-synthase II (called amxFabF), encoded by the anammox-specific gene cluster I, is analogous to FabF enzymes, type II β-ketoacyl-ACP-synthases regulating the canonical fatty acid biosynthesis in bacteria (FAS II). Members of this enzyme family adopt a homomeric configuration with symmetric active sites involved in decarboxylation/ condensation reactions to form the straight chain fatty acid carbon skeleton [4].

With X-ray determination of the crystal structure and biochemical assays, we have demonstrated that amxFabF operates as heterodimer, diverging from the canonical homodimeric configuration of FabF enzymes. This represents a novel model in fatty acid synthesis, being the first type II β-ketoacyl-ACP-synthase known to exhibit a heterodimeric structure and emphasizing the distinctive nature of anammox bacteria metabolism.

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