

## Radical SAM enzymes: Novel catalysts for peptide modification and engineering

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Radical SAM enzymes are an emerging class of enzymes only recently recognized as a super-family (1). These metallo-enzymes which catalyze chemically challenging reactions use a radical-based mechanism to have access to chemistry and transformations not otherwise reachable. Recently, in connection with the progresses in genomic and metagenomic, radical SAM enzymes have been shown to be widespread in natural product biosynthetic pathways including many antibiotics, bacteriocins and anticancer agents. They have been shown to catalyze a broad range of reactions, some of which having no counterparts in synthetic chemistry.

In the last years, radical SAM enzymes have been shown to be instrumental for the biosynthesis of an emerging class of natural products called **RiPPs** "*Ribosomally synthesized and post-translationally modified peptides*" (2). RiPPs are characterized notably by unconventional post-translational modifications many of which including cyclization, epimerization or methyl transfer reactions are catalyzed by radical SAM enzymes.

Recent progresses have been made on these challenging enzymes leading to a deeper understanding of these novel reactions which, in most cases, remain elusive. Notably, we have demonstrated novel enzymatic strategies for peptide methylation (3) and identified novel post-translational modifications leading to the formation of complex peptide structures. These fascinating enzymes represent thus an emerging class of catalysts with an outstanding potential for peptide engineering.

1. Sofia HJ et al. (2001) *Nucleic Acids Res.* **29**, 1097

2. Arnison PG et al. (2013) *Nat. Prod. Rep.* **30**, 108

3. Pierre S et al. (2012) *Nat. Chem. Biol.* **8**, 957