Enzyme-Catalyzed Fluoromethylation

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Strategic fluorination can optimize the pharmacological properties of drugs and lead compounds by modulating their membrane permeability and metabolic stability [1]. Hence, the development of organic fluorides and the methodologies towards fluorination are of great interest [2]. Enzyme-catalyzed fluorination can be an efficient and sustainable method to address this question. In this presentation, we report a system of introducing fluoromethyl group enzymatically, in which *S*-adenosyl methionine (SAM)-dependent methyltransferase are used to transfer fluoromethyl group from *in vitro* generated fluoro-SAM (**Figure 1**) [3]. The described system requires fluoromethyl iodide as a flouromethyl donor, robust bacterial halide methyl transferase, catalytic amount of SAH and methyl transferases that are capable to efficiently transfer fluoromethyl group to different substrates containing *N*-, *C*-, and *O*-nucleophilies. This approach provides innovative biocatalytical method towards fluoromethylation of a wide range of substrates.

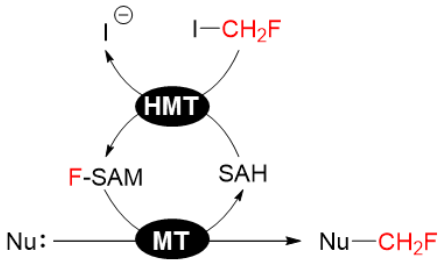

Figure 1. HMT-MT cascade transferring fluoromethyl group to *N*-, *C*- and *O*-nucleophiles.

[1] A. Rentmeister, F. Arnold, R. Fasan, *Nat. Chem. Biol.,* **2009**, *5*, 26-28.
[2] R. Senatore, M. Malik, M. Spreitzer, W. Holzer, V. Pace, *Org. Lett.,* **2020**, *22*, 1345-1349.
[3] J. Peng, C. Liao, C. Bauer, F.P. Seebeck, *Angew. Chem.*, **2021**, *133*, 27384-27389.