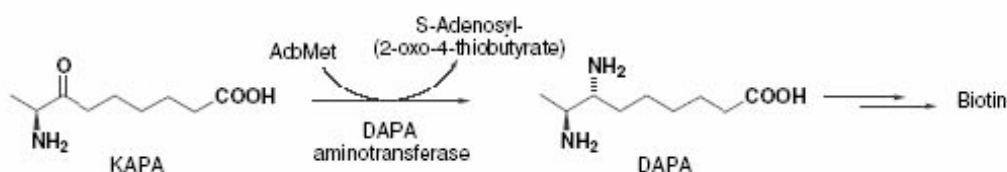


# ***Mycobacterium tuberculosis* DAPA aminotransferase, a potential therapeutic target against tuberculosis**

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Tuberculosis (TB) remains one of the major infectious diseases in the world. Several treatments against *Mycobacterium tuberculosis*, the pathogenic agent, are available. However, the increasing emergence of multi-drug resistant strains (MDR-TB) as well as extreme-drug resistance (XDR-TB) to existing antibiotics requires the discovery of new active molecules. Biosynthesis of biotin is specific to plants and microorganisms. Therefore, the enzymes involved in this pathway are potential targets for the discovery of new antibiotics. Gene inactivation experiments performed on *M. smegmatis* showed that *bioA*, the gene coding for DAPA aminotransferase involved in the biosynthesis of biotin, has been implicated in long-term survival of mycobacteria. Moreover, no gene encoding for a biotin transporter was identified in the annotated genome of *M. tuberculosis*, which leads to hypothesis that this microorganism is reliant on his own biotin production. Therefore the DAPA aminotransferase represents a potential therapeutic target against TB.



In order to find new antibiotics against TB, we cloned and expressed *M. tuberculosis* DAPA aminotransferase in *Escherichia coli*. The enzyme was biochemically characterised and a detailed kinetic study was performed.<sup>2</sup> We also identified a new specific binding mode in the active site for the enantiomer of the substrate KAPA, which behaves as a strong inhibitor. Several simple inhibitors analogous to amiclennomycin, a known inhibitor of DAPA aminotransferase, or to the KAPA substrate were synthesised and characterised. Some of them have a good activity against the model organism *M. smegmatis*. Their activities will be evaluated *in vivo* on *M. tuberculosis*.

1- Keer J, Smeulders MJ, Gray KM, Williams HD, *Microbiology* **2000**, 146, 2209-17  
2- Mann S, Ploux O *FEBS J.* **2006**, 273 4778-4789.

