DOI: 10.46991/JISEES.2025.SI1.014

How FocA Facilitates Fermentation and Respiration of Formate in *Escherichia coli*: Sustainable Formic Acid Production

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ABSTRACT

Formic acid and dihydrogen are important reductants and energy sources for microorganisms. In particular, formic acid is an attractive sustainable storage compound for future use in biofuel cells. Formate is also produced as a fermentation product by many bacteria and archaea, and it can be readily converted to H_2, a fermentation process in the enterobacterium *Escherichia coli*. At physiological pH, formic acid is mainly present as the dissociated formate anion and therefore cannot diffuse freely across the cytoplasmic membrane. Specific and bidirectional translocation of formate across the membrane is, however, achieved in *E. coli* and other microorganisms by the homopentameric membrane protein, FocA (formate channel A). FocA is the archetype of the superfamily of formate-nitrate transporters (FNT), which are found in archaea, bacteria and certain protists, but not in higher eukaryotes. Bidirectional FocA-dependent translocation of formate/formic acid serves to maintain pH homeostasis during fermentation and while efflux of formic acid is by a channel-like mechanism, formate import is coupled to its disproportionation into H_2 and CO_2 by the formate hydrogenlyase (FHL-1) complex. Combined, these channel/transporter-like mechanisms and FHL-1 activity are suggested to help maintain the proton gradient in energy-restricted stationary phase cells. Analysis of amino acid-exchange variants of FocA has yielded insights into the biochemical mechanisms underlying movement of the acid and anion across the membrane. This has led to the identification of a FocA variant with exclusive and very efficient formic acid efflux properties, which has great potential for sustainable, whole-cell formic acid production.

Keywords: formic acid, Bio-H_2, formate translocation, sustainability

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