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Matching the β -oxidation gene repertoire with the wide diversity of fatty acids

Veronica Schiaffi, Frédéric Barras and Emmanuelle Bouveret



Bacteria can use fatty acids (FAs) from their environment as carbon and energy source. This catabolism is performed by the enzymes of the well-known β -oxidation machinery, producing reducing power and releasing acetyl-CoA that can feed the tricarboxylic acid cycle. FAs are extremely diverse: they can be saturated or (poly)unsaturated and are found in different sizes. The need to degrade such a wide variety of compounds may explain why so many seemingly homologous enzymes are found for each step of the β -oxidation cycle. In addition, the degradation of unsaturated fatty acids requires specific auxiliary enzymes for isomerase and reductase reactions. Furthermore, the β -oxidation cycle can be blocked by dead-end products, which are taken care of by acyl-CoA thioesterases. Yet, the functional characterization of the enzymes required for the degradation of the full diversity of FAs remains to be documented in most bacteria.

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Introduction

Fatty acids (FAs) are carboxylic acids with a saturated or (poly)unsaturated aliphatic chain. FAs are the major components of lipids, especially as esters in membrane and storage lipids. However, they can also be found in the environment as their standalone form, such as in the gut where they originate from the degradation of triglycerides found in dietary fats, or as hydrolysis products from host membranes. Most bacteria possess a β -oxidation machinery

allowing use of free FAs from their environment as energy and carbon source. Similar machineries are found in mitochondria. In bacteria, the biochemistry of the degradation process is very well-described [1]. As often, this knowledge derives mainly from studies performed in *E. coli*, and testing only a limited set of saturated or monounsaturated FAs. However, in their environment, bacteria can encounter a diversity of FAs that might be saturated or (poly)unsaturated or have different sizes, and which may require specific enzymatic activities for their degradation. In parallel, bacteria often contain multiple homologs for a given step of the β -oxidation machinery, without a clear understanding of the specific role of these different homologs. Both the diversity of FA degradation enzymes and the role of potential auxiliary enzymes have only been scratched upon in bacteria other than *E. coli*. Therefore, a great variety of functions still await to be discovered.

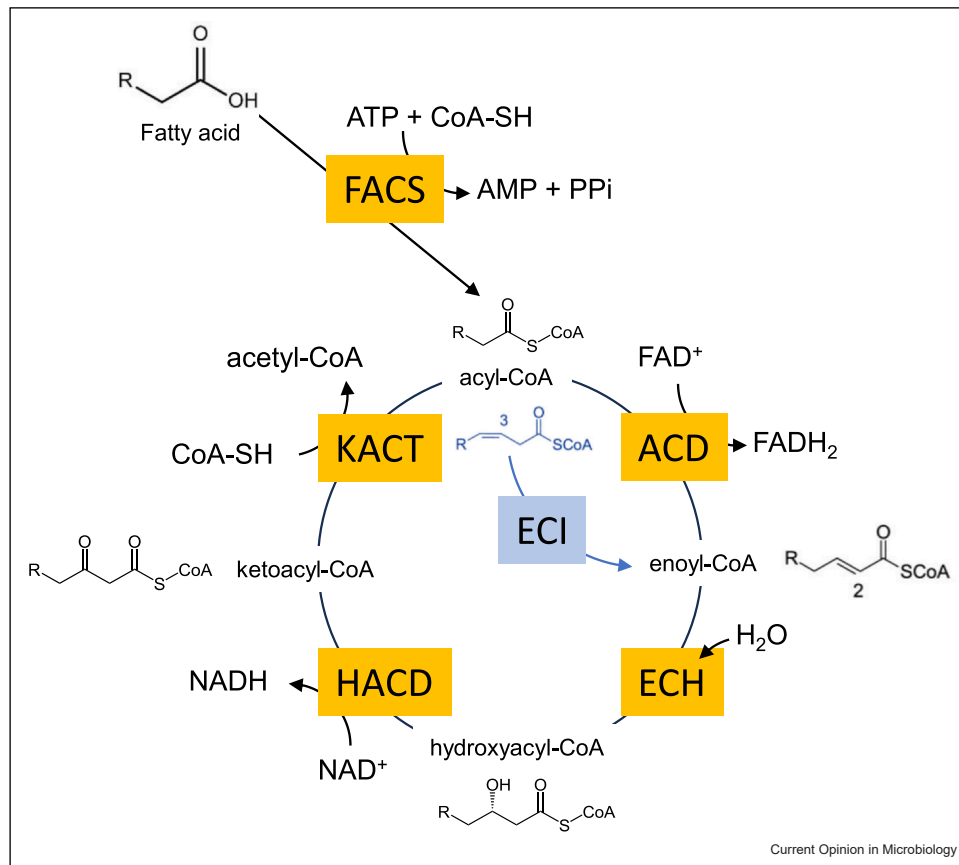
In this review, we report and discuss the information available on the strategies used by bacteria to degrade a wide variety of FAs, especially the unsaturated fatty acids (UFAs). This might prove to be an important resource for biotechnological developments, where the FA degradation machinery has been tweaked in all sorts of fashion for production of biofuel, or of derived molecules of interest [2]. Also, the diversity of FA degradation activities might play a crucial role in the context of the gut microbiome, given the recent reports that bacterial FA metabolism can impact host immunity responses or obesity [3,4]. Finally, recent studies have highlighted the importance of FA degradation for adaptation of pathogenic bacteria to their environment [5,6].

Three main aspects will be discussed: variations observed in the FA degradation enzymes forming the canonical β -oxidation machinery, specific activities required for unsaturated FA degradation (isomerases and reductases), and acyl-CoA (coenzyme A) thioesterase activity required for proofreading and release of dead-end products.

Canonical β -oxidation

The β -oxidation process in bacteria has been reviewed recently in detail [1,7]. Therefore, we will only briefly summarize the canonical β -oxidation cycle involved in the degradation of straight-chain FAs (Figure 1). In Gram-negative bacteria, free FAs are bound and internalized by a specific outer membrane receptor (FadL in *E. coli*). Then, FA import into the cytoplasm is coupled

Figure 1



Canonical β -oxidation of saturated and UFAs at odd position. The enzyme activities are indicated in yellow boxes. ACD : acyl-CoA dehydrogenase. FACS : Fatty acyl-CoA synthase. ECH : enoyl-CoA hydratase. HACD: hydroxyacyl-CoA dehydrogenase. KACT : ketoacyl-CoA thiolase. ECI : 3,2-enoyl-CoA isomerase.

with its activation to acyl-CoA by a fatty acyl-CoA synthase (FACS, FadD in *E. coli*). The acyl-CoA then enters a cycle of successive reactions, acyl-CoA dehydrogenase (ACD), enoyl-CoA hydratase (ECH), hydroxyacyl-CoA dehydrogenase (HACD), and finally ketoacyl-CoA thiolase (KACT), to eventually release 2 carbons in the form of an acetyl-CoA molecule, which then feeds the tricarboxylic acid cycle. The cycle also produces reducing power in the form of FADH₂ and NADH, making growth on long-chain FAs relying heavily on active respiration and a producer of reactive oxygen species [8,9]. Furthermore, the high solicitation of the ubiquinone pool for respiration creates a deficit of ubiquinone available for disulfide bridge formation and thereby triggers an envelope stress response [10,11].

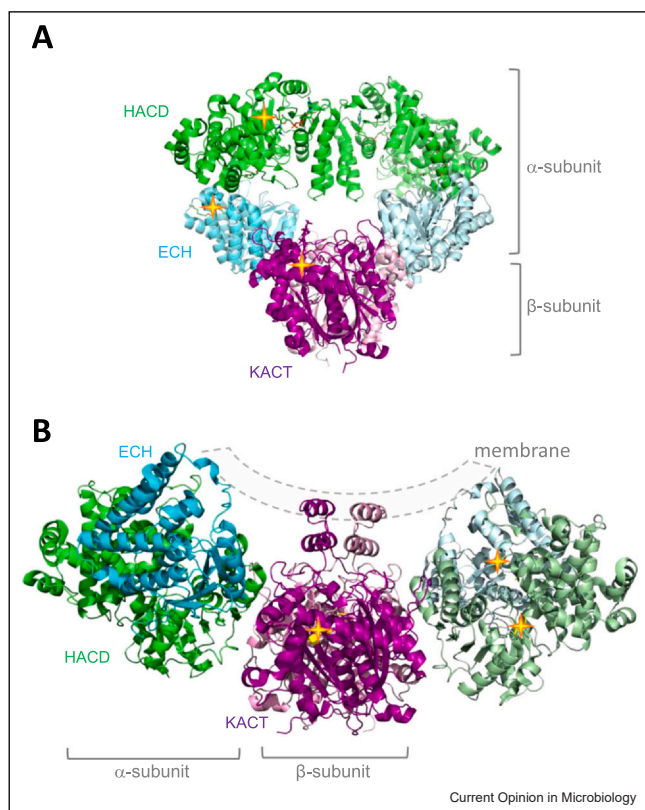
Diversity in the trifunctional enzyme complex family

The trifunctional enzyme complex (TFE) catalyzes three steps of the FA β -oxidation cycle: the ECH, HACD, and KACT reactions. It is formed by a heterotetramer of FadA-like (β -subunit) and FadB-like (α -subunit) proteins (Figure 2). The β -subunit carries the

KACT activity, while the α -subunit carries both the ECH and HACD activities. Phylogenetic studies suggested that TFE can be grouped into 4 families, which might correspond to different quaternary structures [12]. Very often, several TFE homologs are present in the genome of a given species. However, since the sequences alone cannot provide a clue to the TFE(s) responsible for FA degradation, the role of several homologs remains a mystery.

For example, besides the major TFE complex FadBA, *E. coli* also contains a second TFE complex FadIJ (homologs to FadA and FadB, respectively, with roughly 35% identity and 50% similarity for both pairs). The FadIJ enzymes have been proposed to be involved in the anaerobic degradation of FAs due to a residual activity of FadIJ observed in *fadBA* mutants in the absence of oxygen [13]. However, *fadIJ* mutants do not show by themselves any phenotype for growth on FA, neither in the presence or absence of oxygen, and FadBA appears to be the TFE involved in both conditions. Furthermore, *fadBA* and *fadIJ* operons are both repressed in the

Figure 2



Architecture of the TFE complexes. **(a)** Structure of the TFE complex formed by *Pseudomonas fragi* FadBA proteins (PDB: 1WDK) [65]. **(b)** Structure of the TFE complex formed by *E. coli* FadIJ proteins (PDB: 8BNU). This model has been obtained using a combination of the crystallographic structures of FadI and FadJ and the cryo-electron microscopy structure of the complex [15]. The proposed positioning of the membrane is shown in gray. ECH, domain colored in blue. HACD, domain colored in green. KACT, domain colored in purple. Positions of the active sites are indicated by yellow stars. Note that the orientation chosen to show the H–H region of FadI in panel B puts the α -subunit to a 90° rotation compared with the structure shown for FadBA in panel A.

absence of oxygen and induced in the presence of long-chain FAs, suggesting that rather than different growth conditions, they might function together or be involved in the degradation of different kinds of FAs. Consistently, enzymatic kinetic studies suggested they could display different chain size specificity [14]. *In vitro*, FadIJ prefers medium- and long-chain enoyl-CoAs, whereas FadBA prefers short-chain enoyl-CoA substrates [14]. This complementary substrate specificity would allow for complete degradation of long-chain enoyl-CoAs. However, this model is based solely on *in vitro* data and does not fit with the fact that a *fadIJ* mutant does not have a phenotype for growth on long-chain FAs [13]. In addition, structural studies suggest that the FadIJ complex is associated with the

membrane, thanks to the presence of a small H–H region in the β -subunit (FadI), which is absent in FadA [14,15] (Figure 2b). FadIJ structure is indeed more closely related to the human TFE that has been shown also to associate to the membrane through this H–H region [16]. In the absence of *in vivo* phenotype of *fadIJ* mutants, we suggest that FadIJ might be involved in the degradation of specific FA species still to be discovered.

The question of the substrate specificity of TFEs is likely to be a recurring theme. For example, in *Myxococcus xanthus*, 3 operons coding for putative proteins of the TFE family have been identified [17]. Phenotypic analysis has provided evidence of FA degradation activity only for one of them. Similarly, three TFEs have been described in *Streptomyces* [18]. Complementation studies of an *E. coli* *fadBA* mutant suggest that they have different efficiency for FAs of different sizes and are differentially regulated by the presence of FAs or by the growth phase. In *Pseudomonas aeruginosa*, three *fadBA* operons are involved in the degradation of long-chain FAs derived from the lung surfactant phosphatidylcholine [5]. *Pseudomonas putida* possesses two *fadBA*-like operons [19]. The main FadBA system is induced in the presence of FA and is required for the catabolism of n-phenylalkanoic acids [20]. However, a mutant is still able to use FAs, suggesting that the second set is a functional TFE [20]. A last example is the characterization of mutants of the three *fadB* homolog genes in *Ralstonia eutropha* [21].

Diversity in the fatty acyl-CoA synthase and acyl-CoA dehydrogenase families

An even greater number of genes coding for FACS and ACD homologs is often observed in bacterial genomes, suggesting a narrower substrate specificity for these enzymes. For instance, in addition to the FadD acyl-CoA synthase essential for FA degradation, *E. coli* possesses a short-chain acyl-CoA synthase FadK that is expressed in anaerobic conditions [22], but its exact substrate and role *in vivo* are unclear. Likewise, in *P. aeruginosa*, as many as 6 FACS have been reported, all contributing to the degradation of FAs, with some of them specific for acyclic terpenes [23,24]. *Vibrio cholerae* genome encodes two ACD homolog *fadE* genes, both of which being similarly repressed by the FadR regulator in the absence of FAs and activated by the small RNA FarS, suggesting they are both involved in FA degradation [25]. *Pseudomonas putida* KT2440 strain contains at least 5 ACD homologs involved in FA degradation [26,27]. Diversity in the FACS and ACD repertoire is especially impressive for bacteria relying heavily on FA metabolism, such as Mycobacteria containing hundreds of genes potentially involved in FA metabolism [28].

Isomerases involved in the degradation of unsaturated fatty acids

The reactions described in Figure 1 form the canonical β -oxidation cycle required for the degradation of straight-chain saturated FAs. However, a variety of (poly)unsaturated FAs are also metabolized by β -oxidation and require different auxiliary enzymes, depending on the position of the double bond, at an odd or at an even carbon position.

The more ‘classical’ case is the presence of an unsaturation at an odd position, such as the 9-*cis* double bond present in oleic acid and in many other dietary FAs. After 3 cycles of β -oxidation, the 3-*cis* double bond is directly isomerized to 2-*trans* that can be processed further by the ECH hydratase, so that the ACD step is shunted (Figure 1, reaction highlighted in blue). Very often, this 3,2-enoyl-CoA isomerase activity (ECI) is carried out by the same protein that carries the subsequent ECH reaction (such as FadB in *E. coli*). Indeed, these two reactions are performed by enzymes of the same low-similarity hydratase/isomerase superfamily. In the case of ECI/ECH bifunctional enzymes such as FadB, the two reactions share a common catalytic site [29]. However, the ECI reaction might also be carried out by a standalone ECI protein [30]. For instance, in *Mycobacterium tuberculosis*, it has been shown that the FadB enzyme does not perform the ECI reaction because of a steric hindrance caused by the Phe287 residue at the catalytic site [31]. A distinct isomerase is therefore required for the degradation of oleic acid. Several potential ECI proteins have been screened based on their *in vitro* biochemical activity, their upregulation in the presence of unsaturated FAs, and their ability to complement an *E. coli* Δ *fadBA* mutant expressing Mtb FadBA. This led to the characterization of several standalone *cis*–*trans*-enoyl-CoA isomerases and of the prominent monofunctional ECI (EchA5) involved in the degradation of oleic acid [31].

It has to be mentioned that FadB-like enzymes, in addition to the ECH, HACD, and ECI activities described above, possess a fourth activity of 3-hydroxy-acyl epimerase [32]. It may take place when particular types of unsaturated FAs are degraded, but to date, there is no report of such an activity *in vivo*.

2. 2,4-dienoyl-CoA reductase involved in the degradation of unsaturated fatty acids

The degradation of FAs with a double bond at an even position requires an additional enzymatic activity. During the degradation of this class of FAs, after a number of β -oxidation cycles placing the double bond at position 4 and one ACD reaction, a 2,4-double-bound intermediate (*trans*-2,*cis*-/*trans*-4-dienoyl-CoA) is formed (Figure 3a). This intermediate cannot be processed by

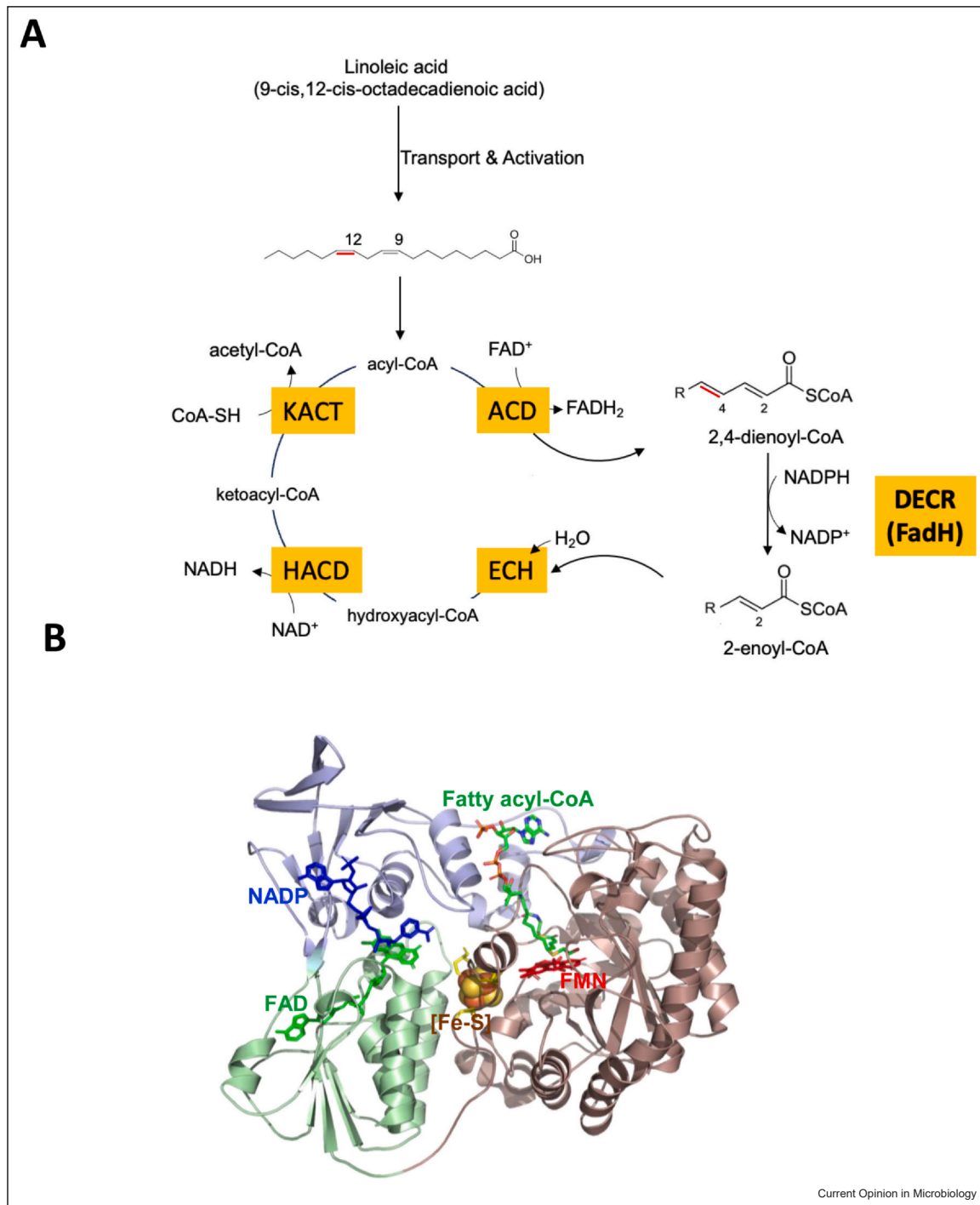
the ECH enzyme [33]. Instead, it must be reduced by an auxiliary 2,4-dienoyl-CoA reductase (DECR) to *trans*-2-enoyl-CoA that can reenter the β -oxidation cycle, allowing the complete degradation of the carbon chain [33].

In bacteria, the reduction of double bonds at an even position of unsaturated FAs is performed mainly by the FadH protein family. *E. coli* FadH is a 73-kDa monomer whose structure has been solved [34] (Figure 3b). FadH is characterized by the presence of three different domains: the N-terminal residues 1–368 form a triosephosphate isomerase barrel that binds FMN, a [4Fe–4S] cluster, and the substrate; residues 369–467 and 626–671 form the FAD-binding site; and residues 468–625 form the NADP(H)-binding domain [34]. The reduction of *trans*-2,*cis*-/*trans*-4-dienoyl-CoA proceeds from NADPH to the substrate by electron transfer through the FAD, the [4Fe–4S] cluster, and FMN to finally reduce the substrate to generate 2-enoyl-CoA that can be processed subsequently by the ECH enzyme [35]. Mutations in the cysteine residues that bind the [4Fe–4S] cluster result in a loss of function of the protein, suggesting that the cluster is essential for a successful electron transfer [36]. Initial studies of FadH enzymatic activity revealed that the protein was lacking stereoselectivity and that it could reduce both the 2-*trans*,4-*cis* and 2-*trans*,4-*trans* isomers with equal efficiency [37]. This suggested a possible isomerization reaction performed by FadH on the substrate, but such an activity was not detected [35].

It is expected that *fadH* would be essential for growth on only FAs with a double bond at even position, but only a few studies have tested its importance *in vivo*. To our knowledge, the only report is in *E. coli*, where a *fadH* mutant has been shown to be affected for growth on petroselinic acid (*cis*-6-octadecenoic acid) but not on oleic acid (*cis*-9-octadecenoic acid) [38]. In other organisms such as *Shewanella livingstonensis* Ac10, FadH might have an indirect role in membrane remodeling in response to stress conditions. Indeed, the marine γ -proteobacteria *S. livingstonensis* Ac10 produces eicosapentaenoic acid (a 20-carbon FA containing 5 double bonds) subsequently incorporated into the membrane lipids to resist to low temperature, high hydrostatic pressure, and oxidative stress. In this bacterium, FadH has a role in the conversion of docosahexaenoic acid into eicosapentaenoic acid, and this conversion has been shown to be drastically impaired in a *fadH* mutant [39].

Interestingly, a bacterium-like DECR enzyme has been discovered in the mitochondria of protozoan parasites belonging to Trypanosoma species [40]. The capability of these parasites to switch from an extracellular to an intracellular lifestyle is associated with genes that have been acquired through lateral gene transfer mostly from

Figure 3



DEC (FadH). **(a)** Degradation of linoleic acid with a double bond at an even position (highlighted in red). After 3 cycles of degradation, 2,4-dienoyl-CoA is produced by ACD. The action of the DEC is required for its conversion to 2-enoyl-CoA that can reenter the cycle. **(b)** Structure of *E. coli* FadH. The N-terminal TIM barrel is colored in pale red, the acyl-CoA substrate is atom color-coded, and FMN cofactor is shown as red sticks. The [4Fe-4S] cluster is in the center of the figure (yellow and orange balls). The middle flavodoxin-like domain is in green, with FAD drawn as green sticks. The C-terminal domain is in blue and includes NADP shown in blue sticks. TIM : triose-phosphate isomerase. Modified from [34].

Proteobacteria. The FadH-like protein found in *Leishmania major* has been acquired likely from *Proteobacteria* during the first evolution stages of Trypanosomas and is highly conserved in the intracellular parasites. *L. major* and *E. coli* FadH enzymes are homologs, with conserved cofactor binding and active sites. A higher expression of FadH is observed in the differentiation from *L. major* extracellular (promastigotes) to intracellular stage (amastigotes) and it is essential for survival inside macrophages and for the virulence during infections in mice models [40]. A deletion of this gene leads to an accumulation of 2,4-dienoyl-CoA that might be toxic for amastigotes, as accumulation of some UFAs shows a great antimicrobial activity [40], or might inhibit the β -oxidation of other FAs as it has been described in mammals [41].

FadH appears to be widely conserved in bacteria [40], which suggests that the presence of a DECR is crucial to deal with the complex nature of FA mixtures found in the environment.

Thioesterases involved in the degradation of unsaturated fatty acids

Acyl-CoA species with double bonds at positions 3 and 5 are another type of intermediates that can be generated through the partial degradation of unsaturated FAs. First, in the case of a double bond at an odd position such as in oleic acid, it has been shown that 10% of the 2,5-dienoyl-CoA is 'mistakenly' isomerized into 3,5-dienoyl-CoA instead of being processed by the ECH [42] (Figure 4a). Second, specific unsaturated FAs such as conjugated linoleic acid will also lead to the formation of 3,5-dienoyl-CoA by their degradation through the canonical β -oxidation cycle (Figure 4b). In *E. coli*, these 3,5-dienoyl-CoA species are dead-end products that cannot be further processed because *E. coli* lacks the activity of 3,5-tetradeca- or 3,5-dodecadienoyl-CoA isomerase [42].

In *E. coli*, the accumulation of the medium-chain 3,5-tetradecadienoyl-CoA or 3,5-dodecadienoyl-CoA intermediates is detrimental since they might both inhibit the enzymes of the FA degradation machinery, and lock and titrate the available CoA molecules. It has been shown however that when *E. coli* is grown on conjugated linoleic acid, free 3,5-tetradecadienoic acid is detected in the growth medium, suggesting that an acyl-CoA thioesterase activity might prevent toxicity of the accumulated intermediate [42]. Furthermore, a thioesterase activity is indeed induced in the presence of FAs [42]. Thioesterases belong to the large hotdog fold protein family and can be involved in a variety of metabolic pathways [43]. The hotdog fold is usually formed by a dimer, while some enzymes such as TesB in *E. coli* present a 'double hotdog' resulting from the fusion of the hotdog domain (Figure 4c) [44]. This protein family

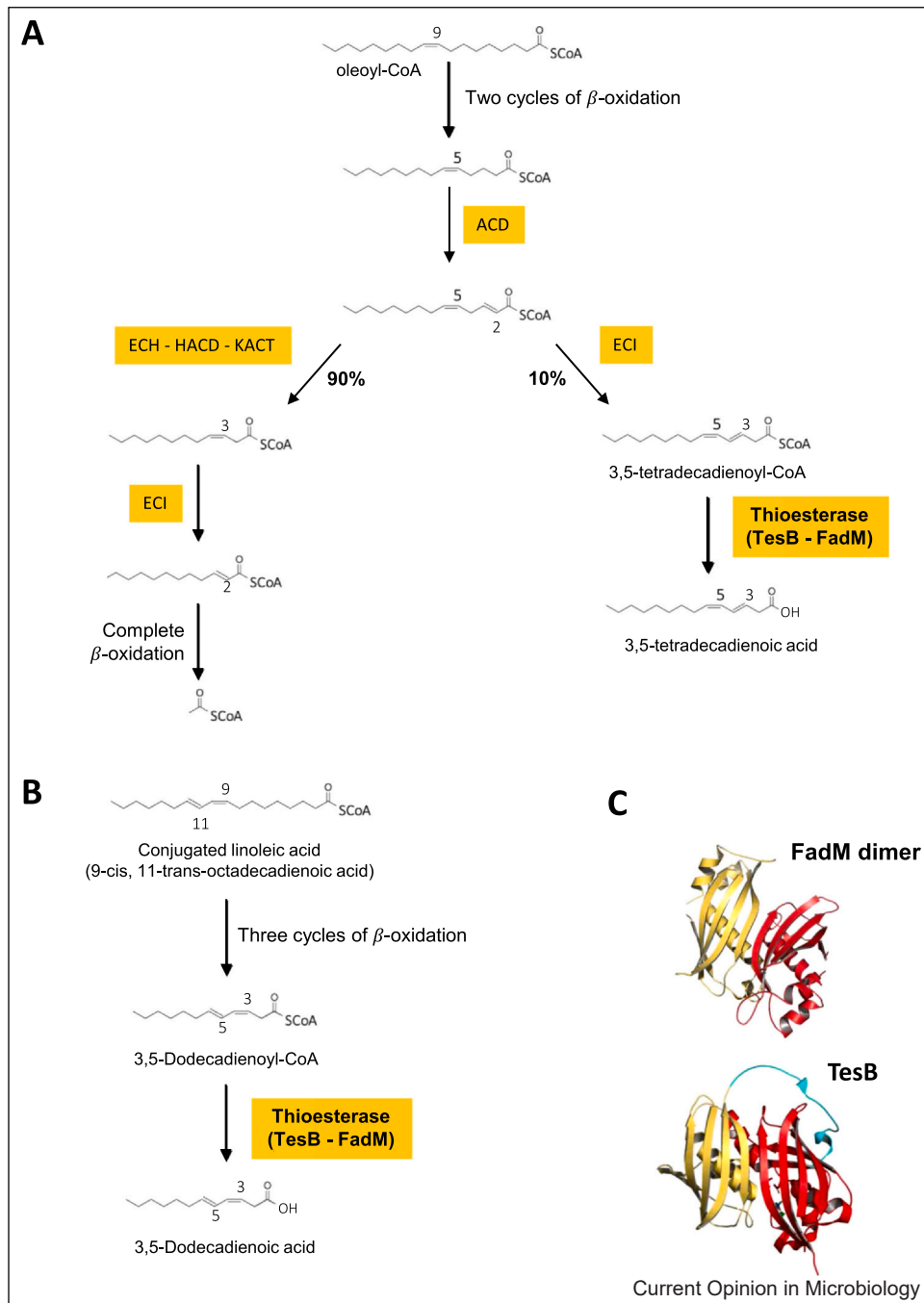
has a low degree of primary sequence conservation, despite the conservation of the hotdog fold observed in the numerous three-dimensional structures available. The catalytic scaffold and residues are not strictly conserved either. This prevents a direct functional assignment from a sequence-based or even three-dimensional structure-based approach [45]. Seven hotdog thioesterases are present in *E. coli*. Three of them have been assigned to specific pathways different from FA metabolism (EntH in enterobactin synthesis, PaaI in phenylacetic degradation, and MenI in the synthesis of menaquinone) [46–48]. YciA thioesterase is active on acyl-CoA and may be involved in CoA recycling and balancing acyl-CoA pools [45]. Three thioesterases have been assigned to the degradation of FAs (TesB, FadM, and YigI). They are active on acyl-CoA, though they seem to have broad specificities and redundant functions [42,49,50]. Most notably, the thioesterases II (TesB) and III (FadM) were found to allow for the partial degradation of conjugated linoleic acid [49] (Figure 4b). *fadM* expression is controlled by the FadR repressor (see below) and is therefore responsible for the observed induction of a thioesterase activity in the presence of exogenous FAs [51]. More recently, the YigI thioesterase has been shown to contribute also to the growth on conjugated linoleic acid [50].

It must be noted that a 3,5-dienoyl-CoA isomerase activity is present in eukaryotes [30]. It is possible that bacteria other than *E. coli* might possess this activity and hence would not require the thioesterase proofreading mechanism discussed above.

A word about regulation

Expression of genes involved in the degradation of FAs is controlled by transcriptional repressor and induced in the presence of exogenous FAs. The best-described regulator is FadR from the GntR protein family, found in *E. coli* and γ -proteobacteria [52]. FadR represses *fad* genes in the absence of exogenous FAs. In the presence of long-chain FAs (more than 12-carbon long), after their import and activation to CoA via FadL and FACS proteins, long-chain acyl-CoA binds to FadR, triggering its release from the DNA and the expression of the *fad* genes. For a detailed description of this FadR-dependent regulation, see [1,53]. Regulators performing a role similar to FadR have been described in other bacteria, even if they belong to the distinct TetR protein family. For example, the YsiA protein of *Bacillus subtilis* controls the expression of a full set of genes involved in FA degradation [54]. A homolog protein has been described in *Thermus thermophilus* [55]. In *P. aeruginosa*, the PsrA protein (also from the TetR protein family) has been shown to repress *fadBA* and *fadE* expression [56,57]. For a global description of the genetic regulation of FA degradation in different bacteria, see reference [58].

Figure 4



Thioesterase-mediated proofreading of dead-end 3,5-dienoyl-CoA intermediates. **(a)** 3,5-tetradecadienyl-CoA is produced by an unspecific isomerase activity during degradation of oleic acid [51]. 3,5-tetradecadienoic acid is released by the activity of thioesterases. **(b)** 3,5-dodecadienyl-CoA is produced by the degradation of conjugated linoleic acid [49,50]. 3,5-dodecadienoic acid is released by the activity of thioesterases. **(c)** Hotdog fold of the FadM dimer (PDB: 1NJK) and of the TesB monomer (PDB: 1C8U) [44]. The two repeats of TesB are highlighted with 2 different colors, connected by a segment colored in blue.

Obviously, the induction of expression in the presence of exogenous FAs is a strong indication that a gene is involved in FA degradation. However, the full set of FA degradation genes is induced in the presence of straight-

chain FAs, even if they are not useful in this condition. For example, in *E. coli*, the genes coding for the auxiliary enzymes FadH and FadM are repressed by FadR and induced in the presence of any long-chain FAs in concert

with the canonical enzymes of the β -oxidation cycle [59,60]. In *Bacillus*, the regulon of the YsiA regulator comprises genes predicted to form the canonical β -oxidation cycle, but also putative homologs and auxiliary enzymes such as FadH [54]. Also, in *Vibrio cholerae*, a putative thioesterase, which might have a role similar to FadM, is controlled by FadR [61]. Therefore, genes that are useless in the presence of saturated FAs, such as *fadM* and *fadH*, are still induced, which might appear as a waste of energy. However, this might be explained by the fact that unsaturated FAs represent the majority of FAs encountered in the environment, and more often in complex mixtures of different types of FAs for which all the panoply of degradation enzymes are required. An unfortunate consequence for the researcher is that genetic regulation cannot be a means of identifying the genes specifically involved in the processing of FAs containing double bonds.

Perspectives and challenges

The challenge is thus to attribute functions to the many homologs of the different steps of β -oxidation found in bacterial genomes. The first approach to systematically identify the enzymes involved in FA catabolism in a bacterium of interest would be to characterize the regulons of FA-sensing regulators. However, it is not possible to simply search for potential binding sites in the genome, because the consensus sites of FadR-like or PsrA-like regulators are notoriously not very well-conserved [52]. For example, new FadR-binding sites that had escaped previous sequence search could be evidenced solely experimentally in *E. coli* [62,63]. Therefore, experimental transcriptomic studies would have to be performed, in the presence of long-chain FAs, or if feasible on mutants for the transcriptional repressors sensing long-chain FAs. This approach was used to identify the last missing gene for β -oxidation in *E. coli* [64]. Such an approach has been successfully used also more recently in *M. tuberculosis* to identify genes involved in degradation of oleic acid among myriad genes encoding proteins with homology to β -oxidation enzymes [31]. However, as discussed above, the identification of genes induced by long-chain FAs will not give information on the precise biochemical function of the cognate enzymes. Another approach for a more systematic prediction of the functions of FA degradation enzymes would be to have access to precise and rigorous classification of subprotein families. However, here again, it is surprising that there are no exhaustive phylogenetic studies of the different enzymes of the β -oxidation cycle and auxiliary enzymes. Only a classification of the TFE enzymes into four groups has been proposed [12], however with no correspondence with distinct

potential biochemical functions. Dedicated and exhaustive phylogenetic studies on the different enzymes involved in FA degradation might prove helpful to predict their possible sequence-function relationship, but also simply to have an idea of the distribution of the different activities in bacteria. However, as exemplified with the TFE families, if experimental biochemical information is lacking, this might still be of limited use. More physiological and biochemical studies are therefore needed to assess the extent of the panoply of enzymes involved in the degradation of the variety of FAs.

Conclusion

The huge diversity of enzymes involved in FA degradation that can be identified in bacterial genomes certainly reflects the adaptation of bacteria to an equally huge diversity of exogenous FAs available in their specific niche. A striking example is *M. tuberculosis* that has been reported to contain hundreds of genes potentially involved in FA metabolism [28]. This certainly reflects the very specific lipid membranes synthesized by Mycobacteria (mycolic acids), but maybe also the FA storage and catabolic activities, including β -oxidation required for its survival inside granuloma. Another example is *P. aeruginosa*, in which the β -oxidation machinery is induced in the lungs of cystic fibrosis patients, to make use of FAs produced through the hydrolysis of phosphatidylcholine from the host [5]. In the case of enteric bacteria, variety in FAs arises directly from diet. Therefore, it is expected that FA catabolism activities will have a strong impact on the gut microbiome. Recent studies indeed reported the effect of mutations in the *fad* genes altering virulence or colonization ability of *Vibrio cholerae* [6].

Thus, in front of the importance of FA catabolism in the physiology of pathogens or in the context of the microbiome, the scarcity of studies to better characterize FA catabolism in bacteria other than *E. coli* is all the more surprising.

Data Availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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