Δ^{12}-fatty-acid desaturase 1.14.19.6

1 Nomenclature

EC number
1.14.19.6

Systematic name
acyl-CoA,hydrogen donor:oxygen Δ^{12}-oxidoreductase

Recommended name
Δ^{12}-fatty-acid desaturase

Synonyms
Δ^{12}Des <29> [28]
Δ^{12} desaturase <7,15> [21,29]
Δ^{12} fatty acid desaturase <1,12,17> [25,27,32]
Δ^{12} oleate hydroxylase <4> (<4> shows Δ^{12} desaturase activities on ^{16}C and ^{18}C monounsaturated fatty acids [26]) [26]
$\Delta^{12}(\omega^6)$-desaturase <11> [13]
Δ^{12}-FAD <25> [22]
Δ^{12}-desaturase <29> [28]
Δ^{12}-desaturase system | <3> (<3> enzymatic complex [9]) [9]
Δ^{12}-fatty acid desaturase <15,25> [5,22]
Δ^{12}-fatty acyl-CoA desaturase <11> [13]
Δ^{12}DS <24> (<24> bifunctional enzyme with strong Δ^{12} and low Δ^{15} desaturase activities [16]) [16]
FAD2 <5,10,12,17,28,30> (<10> Δ^{12} fatty acid desaturase 2 [15]) [15,24,27,30,31,32]
FAH <4> [26]
Fm2 <23> [18]
KlFAD2 <12> [20]
Le-FAD2 <21> [17]
PtFAD2 <11> [13]
PtFAD6 <11> [13]
Δ^{12} fatty acid desaturases <28> [24]
Δ^{12} fatty acid desaturase <30> [30]
fatty acid desaturase-2 <5> [31]
oleoyl coenzyme A desaturase <11> [13]
oleoyl-CoA Δ^{12} desaturase <11> [13]
oleoyl-Δ^{12} desaturase <26> [23]
oleoyl-Δ^{12}/linoleoyl-Δ^{3} desaturase <27> [23]

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2 Source Organism

<1> *Arachis hypogaea* [25]
<2> *Caenorhabditis elegans* [2]
<3> *Lipomyces starkeyi* [9]
<4> *Claviceps purpurea* [26]
<5> *Gossypium hirsutum* [31]
<6> *Chlorella vulgaris* [8]
<7> *Hevea brasiliensis* [21]
<8> *Acanthamoeba castellanii* [7,10]
<9> *Aspergillus parasiticus* [1]
<10> *Linum usitatissimum* [15]
<11> *Phaeodactylum tricornutum* [13]
<12> *Kluyveromyces lactis* [20,32]
<13> *Synechococcus sp. PCC 7002* [11]
<14> *Periplaneta americana* [3,6]
<15> *Mortierella alpina* [5,29]
<16> *Borago officinalis* [12]
<17> *Lachancea kluyveri* [27]
<18> *Cadra cautella* [4]
<19> *Spinacia oleracea* (UNIPROT accession number: Q8H943) [14]
<20> *Acheta domesticus* [6]
<21> *Lentinula edodes* (UNIPROT accession number: Q65YX3) [17]
<22> *Umbelopsis isabellina* (UNIPROT accession number: P59668) [19]
<23> *Gibberella moniliformis* (UNIPROT accession number: Q27ZJ7) [18]
<24> *Coprinopsis cinerea* (UNIPROT accession number: $A2A_1C4$) [16]
<25> *Triadica sebifera* (UNIPROT accession number: A5J295) [22]
<26> *Emericella nidulans* (UNIPROT accession number: Q5BEJ3) [23]
<27> *Emericella nidulans* (UNIPROT accession number: Q5AWX6) [23]
<28> *Gossypium hirsutum* (UNIPROT accession number: Q8W2B9) [24]
<29> *Acheta domesticus* (UNIPROT accession number: B7SB91) [28]
<30> *Gossypium hirsutum* (UNIPROT accession number: B0FYE4) [30]

3 Reaction and Specificity

Catalyzed reaction
acyl-CoA + reduced acceptor + O_2 = Δ^{12}-acyl-CoA + acceptor + 2 H_2O

Natural substrates and products
S (Z)-9-tetradecenoic acid + ? <18> (<18> biosynthetic pathway for producing the sex pheromone component (Z,E)-9,12-tetradecadienyl acetate in moths involves a Δ^{12} desaturase [4]) (Reversibility: ?) [4]

P tetradec-9,12-dienoic acid
S cis-9-octadecenoic acid + reduced acceptor + O_2 <11> (<11> PtFAD2 is involved in the biosynthesis of eicosapentaenoic acid [13]) (Reversibility: ?) [13]
P cis,cis-9,12-octadecadienoic acid + acceptor + H_2O
S oleic acid + ? <9,10,12,21,23,24> (<9> Δ^{12}-desaturase mutant shows delayed spore germination, a twofold reduction in growth, a reduced level of conidiation and complete loss of sclerotial development, compared with the wild-type enzyme [1]; <21> expression in Saccharomyces cerevisiae leads to endogenous production of linoleic acid [17]; <23> linoleic acid was detectable when expressing Fm2 in Δ^{12} desaturase knockout Yarrowia lipolytica [18]) (Reversibility: ?) [1,15,16,17,18,20]
P linoleic acid + ?
S oleoyl-CoA + reduced acceptor + O_2 <1,26,27> (Reversibility: ?) [23,25]
P 9,12-octadecadienoyl-CoA + acceptor + H_2O
S oleoyl-CoA + reduced acceptor + O_2 <14> (<14> the Δ^{12} desaturase provides the key step for the cockroach to become nutritionally independent of dietary lipid and to synthesize eicosanoids de novo [3]) (Reversibility: ?) [3]
P octadec-9,11-dienoyl-CoA + acceptor + H_2O
S Additional information <8,11,13> (<8> oxygen availability alone can regulate de novo Δ^{12}-desaturase synthesis in Acanthamoeba castellanii and oxygen can limit the activity of preexisting Δ^{12}-desaturase [10]; <11> PtFAD6 is involved in the biosynthesis of hexadecantrienic acid [13]; <13> synergistic effect of high-light and low temperature on cell growth of the Δ^{12} fatty acid desaturase mutant [11]; <8> the main transition in fatty acid metabolism of Acanthamoeba castellanii during batch growth appears to be primarily related to a rapid decline in Δ^{12}-desaturase activity after 24 h. The resultant large growth-dependent changes in the degree of fatty acid unsaturation would be expected to affect the physical state and/or fluidity of membranes, and may be related to many of the distinctive physiological and biochemical characteristics displayed by Acanthamoeba castellanii in different stages of batch growth [7]) (Reversibility: ?) [7,10,11,13]
P ?

Substrates and products

S (Z)-9-tetradecenoic acid + ? <18> (<18> biosynthetic pathway for producing the sex pheromone component (Z,E)-9,12-tetradecadienyl acetate in moths involves a Δ^{12} desaturase [4]) (Reversibility: ?) [4]
P tetradec-9,12-dienoic acid
S 5,8,11,14-eicosadecatetraenoyl-CoA + reduced acceptor + O_2 <26,27> (Reversibility: ?) [23]
P 5,8,11,14,17-eicosadecapentaenoyl-CoA + acceptor + H_2O
S 6,9,12-octadecatrienoyl-CoA + reduced acceptor + O_2 <26,27> (Reversibility: ?) [23]
P 6,9,12,15-octadecatetraenoyl-CoA + acceptor + H_2O

S 9,12-octadecadienoyl-CoA + reduced acceptor + O_2 <26,27> (<26,27> high activity [23]) (Reversibility: ?) [23]
P 9,12,15-octadecatrienoyl-CoA + acceptor + H_2O
S 9-hexadecenoyl-CoA + reduced acceptor + O_2 <26,27> (<26,27> low activity [23]) (Reversibility: ?) [23]
P 9,12-hexadecadienoyl-CoA + acceptor + H_2O
S 9-octadecenoyl-CoA + reduced acceptor + O_2 <26,27> (Reversibility: ?) [23]
P 9,12-octadecadienoyl-CoA + acceptor + H_2O
S acyl-CoA + reduced acceptor + O_2 <26,27> (Reversibility: ?) [23]
P Δ^{12}-acyl-CoA + acceptor + H_2O
S cis-7-hexadecenoic acid + reduced acceptor + O_2 <11> (<11> 5.2% desaturation [13]) (Reversibility: ?) [13]
P cis,cis-7,10-hexadecadienoic acid + acceptor + H_2O
S cis-9-heptadecenoic acid + reduced acceptor + O_2 <11> (<11> 22.3% desaturation [13]) (Reversibility: ?) [13]
P cis,cis-9,12-heptadecadienoic acid + acceptor + H_2O
S cis-9-hexadecenoic acid + reduced acceptor + O_2 <11> (<11> 14.7% desaturation [13]; <11> 70.3% desaturation [13]) (Reversibility: ?) [13]
P cis,cis-9,12-hexadecadienoic acid + acceptor + H_2O
S cis-9-icosenoic acid + reduced acceptor + O_2 <11> (<11> 4.1% desaturation [13]) (Reversibility: ?) [13]
P cis,cis-11,14-icosadienoic acid + acceptor + H_2O
S cis-9-octadecenoic acid + reduced acceptor + O_2 <11> (<11> PtFAD2 is involved in the biosynthesis of eicosapentaenoic acid [13]; <11> 20.6% desaturation [13]; <11> cis-9-octadecenoic acid is the most efficient substrate for PtFAD2, 50.3% desaturation [13]) (Reversibility: ?) [13]
P cis,cis-9,12-octadecadienoic acid + acceptor + H_2O
S oleic acid + ? <9,10,12,21,23,24> (<9> Δ^{12}-desaturase mutant shows delayed spore germination, a twofold reduction in growth, a reduced level of conidiation and complete loss of sclerotial development, compared with the wild-type enzyme [1]; <21> expression in Saccharomyces cerevisiae leads to endogenous production of linoleic acid [17]; <23> linoleic acid was detectable when expressing Fm2 in Δ^{12} desaturase knockout Yarrowia lipolytica [18]) (Reversibility: ?) [1,15,16,17,18,20]
P linoleic acid + ?
S oleic acid + reduced acceptor + O_2 <4,5,9,12,15,22,28,29,30> (<5> FAD2 introduces a double bond in position Δ^{12} in oleic acid (18:1) to form linoleic acid (18:2 n-6) [31]) (Reversibility: ?) [1,19,24,26,28,29,30,31,32]
P linoleic acid + acceptor + H_2O
S oleoyl-CoA + reduced acceptor + O_2 <1,26,27> (Reversibility: ?) [23,25]
P 9,12-octadecadienoyl-CoA + acceptor + H_2O
S oleoyl-CoA + reduced acceptor + O_2 <14> (<14> the Δ^{12} desaturase provides the key step for the cockroach to become nutritionally independent of dietary lipid and to synthesize eicosanoids de novo [3]) (Reversibility: ?) [3]
P octadec-9,11-dienoyl-CoA + acceptor + H_2O

S palmitoleic acid + reduced acceptor + O_2 <4> (Reversibility: ?) [26]
P hexa-deca-9,12-dienoic acid + acceptor + H_2O
S Additional information <3,8,11,13,24,25,26,27> (<8> oxygen availability alone can regulate de novo Δ^{12}-desaturase synthesis in Acanthamoeba castellanii and oxygen can limit the activity of preexisting Δ^{12}-desaturase [10]; <11> PtFAD6 is involved in the biosynthesis of hexadecantrienic acid [13]; <13> synergistic effect of high-light and low temperature on cell growth of the Δ^{12} fatty acid desaturase mutant [11]; <8> the main transition in fatty acid metabolism of Acanthamoeba castellanii during batch growth appears to be primarily related to a rapid decline in Δ^{12}-desaturase activity after 24 h. The resultant large growth-dependent changes in the degree of fatty acid unsaturation would be expected to affect the physical state and/or fluidity of membranes, and may be related to many of the distinctive physiological and biochemical characteristics displayed by Acanthamoeba castellanii in different stages of batch growth [7]; <11> no activity with cis-13-docosenoic acid [13]; <3> the Δ^{12}-desaturase enzymatic complex shows a preference towards oleoyl-CoA versus elaidoyl-CoA. Study of substrate specificity of the Δ^{12} desaturase system is difficult due to the involvement of numerous enzymes. At least two activities are involved: in a first step, acyl CoA synthetase catalyzes the formation of oleoyl-CoA from olic acid and CoA, then oleoyl-CoA is desaturated into linoleoyl-CoA. No desaturation occurs when CoA is absent in the reaction medium [9]; <25> gene Ssd12 encodes a Δ^{12}-FAD, which can convert 16:1 and 18:1 into 16:2 and 18:2 fatty acids, substrate specificity, overview [22]; <27> one of two membrane-bound fatty acid desaturases occurring in Aspergillus nidulans, a processive bifunctional oleoyl-Δ^{12}/linoleoyl-Δ^{3} desaturase, substrate specificity of the recombinant enzyme, overview [23]; <26> one of two membrane-bound fatty acid desaturases occurring in Aspergillus nidulans, a strictly monofunctional oleoyl-Δ^{12} desaturase, substrate specificity of the recombinant enzyme, overview [23]; <24> the enzyme is a bifunctional fatty acid desaturase with both high Δ^{12} desaturase activity and unusual Δ^{15} desaturase activities [16]) (Reversibility: ?) [7,9,10,11,13,16,22,23]
P ?

Inhibitors

EDTA <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
Hg^{2+} <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
N-bromosuccinimide <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
N-ethyl-5-phenylisoxazolium 3'-sulfonate <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
NEM <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
iodine <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
iodoacetic acid <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]
trifluoroacetic acid <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]

Metals, ions
Mg^{2+} <3> (<3> activation, Δ^{12}-desaturase system, enzymatic complex [9]) [9]
Mn^{2+} <3> (<3> activation, Δ^{12}-desaturase system, enzymatic complex [9]) [9]
Zn^{2+} <3> (<3> activation, Δ^{12}-desaturase system, enzymatic complex [9]) [9]

Specific activity (U/mg)
Additional information <21,22> (<22> optimal condition for expressing Δ^{12}-fatty acid desaturase in Saccharomyces cerevisiae is 3% galactose induction for 24 h at 15°C [19]; <21> the proportion of linoleic acid in the total fatty acids produced by transformed Saccharomyces cerevisiae increases from 1.1 mol% when grown at 30°C to 2.9 mol% when grown at 15°C [17]) [17,19]

pH-Optimum
7-8 <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]

Temperature optimum (°C)
20 <1> (<1> assay at [25]) [25]
40 <3> (<3> Δ^{12}-desaturase system, enzymatic complex [9]) [9]

4 Enzyme Structure

Molecular weight
43000 <22> (<22> SDS-PAGE of cell membranes of transformed Escherichia coli [19]) [19]

Subunits
? <1> (<1> x * 43000, recombinant enzyme, SDS-PAGE [25]) [25]

5 Isolation/Preparation/Mutation/Application

Source/tissue
cell culture <8> [7]
cotton fiber <30> [30]
cotyledon <28> (<28> very low expression level in roots [24]) [24]
epidermis <14> (<14> low activity [3]) [3]
fat body <14> (<14> most of the activity [3]) [3]
flower bud <30> [30]
fruitbody <21> (<21> 4.2fold increase in mRNA level in mature fruiting bodies compared to mycelium [17]) [17]
hypocotyl <30> [30]
leaf <28,30> (<28> very low expression level in new leaves [24]) [24,30]
mycelium <21> (<21> 3.5fold increase in mRNA level in fruiting body primordia and 4.2fold increase in mRNA level in mature fruiting bodies compared to mycelium [17]) [17]

primordium <21> (<21> 3.5fold increase in mRNA level in fruiting body primordia compared to mycelium [17]) [17]
root <28,30> [24,30]
sclerotium <4> [26]
seed <9,16,25> (<25> composition of major fatty acids in Sapium sebiferum seeds, overview [22]) [1,12,22]
stem <30> [30]
Additional information <10,14> (<14> no activity in thorax and gut tissue [3]; <10> high expression level in bolls between 12 and 16 days after anthesis [15]) [3,15]

Localization

chloroplast <30> (<30> endomembrane network-like distribution around chloroplasts [30]) [30]
cytoplasm <30> [30]
endoplasmic reticulum <14,20> [6]
membrane <16,26,27> (<16> bound to, solubilization of membrane bound enzyme [12]) [12,23]
microsome <3,8,11,14,16> (<8> enzyme activity is increased by up to 10fold during aeration of cultures [10]; <8> greatest in microsomal membranes isolated from early-exponential to mid-exponential phase cells, declines by approximately 50% as cultures progress towards stationary phase [7]; <3> localization of the Δ^{12}-desaturase system [9]; <11> PtFAD2 [13]) [3,7,9,10,12,13]
plastid <11> (<11> PtFAD6 [13]) [13]

Purification

<1> (soluble recombinant enzyme from Escherichia coli strains JM109 and BL21(DE3)) [25]

Cloning

<1> (DNA and amino acid sequence determination and analysis, high level expression in Escherichia coli strains JM109 and BL21(DE3)) [25]
<2> (expression in Saccharomyces cerevisiae) [2]
<4> (expressed in Saccharomyces cerevisiae and in Arabidopsis thaliana) [26]
<5> (expressed in Mus musculus strains C57BL/6 and DBA/2) [31]
<7> (expression in Saccharomyces cerevisiae strain BYdesa) [21]
<11> (heterologous expression in yeast Saccharomyces cerevisiae and Synechococcus) [13]
<12> (expressed in Saccharomyces cerevisiae) [32]
<12> (expression in Saccharomyces cerevisiae strain YHU3046-4A results in endogenous production of linoleic acid, increasement in production of linoleic acid from 0.66 to 1.19 microg/mg dry cell weight when 0.5 microM oleic acid as a substrate was exogenously added) [20]
<15> (heterologous expression in Saccharomyces cerevisiae and Aspergillus oryzae) [5]
<17> (expressed in Saccharomyces cerevisiae strain IFO10150) [27]

<19> (functional expression of a Δ^{12} fatty acid desaturase gene from Spinacia oleracea in transgenic Sus scrofa. Levels of linoleic acid (18:2n-6) in adipocytes that have differentiated in vitro from cells derived from the transgenic pigs are about 10times higher than those from wild-type pigs. In addition, the white adipose tissue of transgenic pigs contained about 20% more linoleic acid (18:2n-6) than that of wild-type pigs) [14]
<21> (expression in Saccharomyces cerevisiae leads to endogenous production of linoleic acid, the proportion of linoleic acid in the total fatty acids produced by transformed Saccharomyces cerevisiae increases from 1.1 mol% when grown at 30°C to 2.9 mol% when grown at 15°C) [17]
<22> (expression of Δ^{12}-fatty acid desaturase genes in Escherichia coli strain BL21 and Saccharomyces cerevisiae strain IN-VSc1 leads to production of an active enzyme which converts 17.876% and 17.604% of oleic acid to linoleic acid, GC-MS detection in vitro and in vivo) [19]
<23> (expressed in wild-type Yarrowia lipolytica and its Δ^{12} desaturase knockout mutant, 62.6 weight percent of total fatty acid was linoleic acid produced in the mutant) [18]
<24> (expressed in Saccharomyces cerevisiae EH1315, 7.9% oleic acid and 29% linoleic acid in yeast expressing Δ^{12} desaturase compared with 37% oleic acid and no detectable linoleic acid in control yeast, fatty acid composition analyzed by gas-liquid chromatography) [16]
<24> (gene Cop-odeA, DNA and amino acid sequence determination and analysis, functional expression in Saccharomyces cerevisiae strain EH1315) [16]
<25> (gene Ssd12, DNA and amino acid sequence determination and analysis, two genomic copies, expression in Saccharomyces cerevisiae) [22]
<26> (gene An2, DNA and amino acid sequence determination and analysis, functional expression in Arabidopsis thaliana) [23]
<27> (gene An1, DNA and amino acid sequence determination and analysis, functional expression in Arabidopsis thaliana) [23]
<29> (expressed in Saccharomyces cerevisiae) [28]
<30> (expressed in Saccharomyces cerevisiae and in the Arabidopsis thaliana fad2-1 mutant (knockout mutants lacking the single FAD2 gene)) [30]

Engineering

Additional information <7,15,24,27> (<24> a recombinant Saccharomyces cerevisiae strain EH1315 expressing gene Cop-odeA accumulates four additional fatty acids identified as 9,12-hexadecadienoic acid, 9,12,15-hexadecatrienoic acid, linoleic acid, and alinolenic acid, which comprised 8.8%, 1.0%, 29.0%, and 0.6% of the total fatty acids, respectively, overview [16]; <7> a transgenic Saccharomyces cerevisiae strain BYdesa, expressing the enzyme from Helvea brasiliensis, produces up to 15% polyunsaturated fatty acids, mostly 9Z,12Z-C18:2, linoleic acid, but also 9Z,12Z-C16:2 fatty acid under inducing conditions, production of 4-hydroxy-2-nonenal, one of the major end products of n-6 polyunsaturated fatty acid peroxidation. Desaturase expression causes adaptation to oxidative stress but not to hyperosmotic stress, phenotype, overview [21]; <27> the seed oil fatty acid composition of Arabi-

dopsis plants expressing An1 is altered, overview [23]; <15> the Δ^{12} desaturase-defective mutant, Mut48, derived from Mortierella alpina 1S-4 produces several fatty acids of the n-9 family such as 6,9-octadecadienoic acid (18:2n-9), 8,11-eicosadienoic acid (20:2n-9), and mead acid. The mutants SR88 and TM912 exhibit a complete Δ^{12} desaturation deficiency with no arachidonic acid accumulation [29]) [16,21,23,29]

Application

nutrition <19> (<19> after functional expression of a Δ^{12} fatty acid desaturase gene from Spinacia oleracea in transgenic Sus scrofa levels of linoleic acid (18:2n-6) in adipocytes that have differentiated in vitro from cells derived from the transgenic pigs are about 10 times higher than those from wild-type pigs. In addition, the white adipose tissue of transgenic pigs contained about 20% more linoleic acid (18:2n-6) than that of wild-type pigs. These results demonstrate the functional expression of a plant gene for a fatty acid desaturase in mammals, opening up the possibility of modifying the fatty acid composition of products from domestic animals by transgenic technology, using plant genes for fatty acid desaturases [14]) [14]

References

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