

Improved methods and cells for increasing enzyme activity and production of insect pheromones

Technical field

5 The present invention relates to methods for increasing enzymatic activity, as well as to methods for production of compounds comprised in pheromones, in particular moth pheromones, such as saturated and desaturated fatty alcohols, saturated and desaturated fatty acids and saturated and desaturated fatty alcohol acetates, and derivatives thereof, in a cell.

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Background

Integrated Pest Management (IPM) is expected to play a major role for both increasing the crop yield and for minimizing environmental impact and enabling organic food production. IPM employs alternative pest control methods, such as mating disruption
15 using pheromones, mass trapping using pheromones, beneficial insects, etc. Pheromones constitute a group of diverse chemicals that insects (like other organisms) use to communicate with individuals of the same species in various contexts, including mate attraction, alarm, trail marking and aggregation. Insect pheromones associated with long-range mate finding are already used in agriculture and forestry applications
20 for monitoring and control of pests, as a safe and environmentally friendly alternative to pesticides. The biological production of pheromones for use pest control is advantageous over chemical synthesis in respect to price, specificity, and environmental impact.

25 Type I pheromones of the moth order Lepidoptera are unsaturated fatty alcohols, aldehydes, or acetates of 10 to 18 carbon chain length. The receptors in male moth antennae are selective for pheromones with a specific chain length, desaturation at a specific carbon in right stereoisomery (Z or E confirmation of double bond), and terminal functional group (Tupec, Bucek, Valterova, & Pichova, 2017). Several
30 biosynthetic enzymes contribute to pheromone production, including fatty acyl-CoA desaturases and fatty acyl-CoA reductases. The desaturases introduce double-bonds into a fatty acyl-CoA. They are thought to be integral membrane proteins receiving electrons from NADH supplied by cytochrome b5 reductase and cytochrome b5. The fatty acyl reductases convert saturated or desaturated fatty acyl-CoA's into saturated or

desaturated fatty alcohols. These enzymes are also integral membrane proteins but are thought to receive electrons directly from NADPH.

Besides the “classic” single-domain membrane-bound cytochrome b5 reductase (CytB5Red) and cytochrome b5 (CytB5), another flavoheme reductase named
5 NAD(P)H cytochrome b5 oxidoreductase (Ncb5or; also known as cytochrome b5 reductase 4 or Cyb5R4) is highly conserved in the animal kingdom. Ncb5or enzymes are distinct from classic CytB5Red/CytB5 pairs, as Ncb5ors contain three domains: a cytochrome b5-like domain, a cytochrome b5 reductase-like domain, and CHORD-
10 SGT1 (CS domain) (Deng, et al., 2010) (see Figure 1). The CS domain occurs in many diverse proteins and was proposed to be involved in protein-protein interaction (Benson, et al., 2019; Zhu, et al., 2004). The Ncb5or CytB5Red-like domain contains multiple insertions and deletions in comparison with CytB5Red (Benson et al., 2019). The same is true for the CytB5-like domain (Figure 2), (Benson et al., 2019). Ncb5ors
15 are believed to have a fundamentally different mechanism for electron transfer compared to the CytB5Red/CytB5 system (Benson et al., 2019). Furthermore, they have an unusual ability to utilize both NADH and NADPH (Benson et al., 2019).

Soluble Ncb5or have been mainly studied in mice or human cells line where knockouts
20 of Ncb5or have led to a reduction in $\Delta 9$ desaturation (Zambo, et al., 2020; Larade, et al., 2008). To date, there are to the best of our knowledge no descriptions of Ncb5or genes or their functions in insects.

Summary

The invention is as defined in the claims.

Herein is provided a cell expressing:

- 5 i) a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate and a desaturated fatty acyl-CoA; and
- ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);
- 10 whereby the cell is capable of producing the compound with a higher titer and/or purity compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

Also provided herein is a cell expressing:

- 15 i) a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a desaturated fatty acyl-CoA and a desaturated fatty acid; and
- ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);
- 20 whereby the cell is capable of producing the compound with a higher titer and/or purity compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

Further provided herein is a method for increasing the activity of at least one enzyme selected from the group consisting of desaturases and fatty acyl CoA reductases (FARs), said method comprising the steps of:

- 25 a. providing a desaturase capable of introducing at least one double bond in a fatty acyl-CoA, thereby converting at least part of said fatty acyl-CoA to a desaturated fatty-acyl-CoA; and/or
- 30 b. providing a FAR capable of converting at least part of said desaturated fatty acyl-CoA to a desaturated fatty alcohol, thereby producing said desaturated fatty alcohol; and
- c. contacting said desaturase and/or FAR with an Ncb5or, thereby increasing the activity of said desaturase and/or FAR compared to the activity of said

desaturase and/or FAR in the absence of said Ncb5or, wherein the activity is measured under the same conditions;
wherein the increase in activity is measured by measuring the concentration of product formed by the desaturase and/or the FAR.

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Also provided herein is a method for production of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA in a cell, said method comprising the steps of:

- a. providing a cell and incubating said cell in a medium; and
- 10 b. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- c. expressing in said cell an Ncb5or;
- d. optionally, recovering said compound.

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Further provided herein is a method for increasing the titer and/or purity of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:

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- a. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- b. expressing in said cell an Ncb5or, thereby increasing the titer and/or purity of
25 said compound compared to the titer and/or purity from a cell not expressing said Ncb5or in the same conditions;
- c. optionally, recovering said compound.

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Also provided herein is a system of nucleic acid constructs comprising nucleic acids encoding an Ncb5or and:

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- a. a desaturase capable of introducing at least one double bond in a fatty acyl-CoA; and/or
- b. a fatty acyl CoA reductase FAR capable of converting at least part of a desaturated fatty acyl-CoA to a desaturated fatty alcohol.

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Further provided herein is a kit of parts comprising:

- a. a cell as provided in the present application;
- b. a nucleic acid system as provided in the present application, wherein said construct is for modifying a cell;
- 5 c. instructions for use; and
- d. optionally, the cell to be modified.

Also provided herein is the use of an Ncb5or in a method for increasing the activity of one or more enzymes.

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Further provided herein is a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde, a desaturated fatty acid and/or a saturated fatty aldehyde obtainable by the methods of the present application.

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Also provided herein is the use of a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde, a desaturated fatty acid and/or a saturated fatty aldehyde obtainable by the methods of the present application.

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Further provided herein is a method of monitoring the presence of pest or disrupting the mating of pest, said method comprising the steps of:

- a. producing a desaturated fatty alcohol and optionally a desaturated fatty alcohol acetate and/or a desaturated fatty aldehyde according to the methods of the present application; and
- 25 b. formulating said fatty alcohol and optionally said fatty alcohol acetate and/or said desaturated fatty aldehyde as a pheromone composition; and
- c. employing said pheromone composition as an integrated pest management composition.

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Also provided herein is a fermentation broth containing the yeast cell according to the present application.

Further provided herein is a fermentation system or a catalytic system comprising the yeast cell according to the present application.

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Also provided herein is a device, such as a pheromone dispenser, for diffusing a pheromone composition, said pheromone composition comprising the desaturated fatty alcohol and/or the desaturated fatty alcohol acetate and/or the desaturated fatty aldehyde obtainable by the methods of the present application.

Further provided herein is a method for producing at least 1 mg/L of a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde and/or a saturated fatty aldehyde in a cell, such as at least 1.5 mg/L, such as at least 5 mg/L, such as at least 10 mg/L, such as at least 25 mg/L, such as at least 50 mg/L, such as at least 100 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at least 750 mg/L, such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L, such as at least 4 g/L, such as at least 5 g/L, such as at least 6 g/L, such as at least 7 g/L, such as at least 8 g/L, such as at least 9 g/L, such as at least 10 g/L, such as at least 11 g/L, such as at least 12 g/L, such as at least 13 g/L, such as at least 14 g/L, such as at least 15 g/L, such as at least 16 g/L, such as at least 17 g/L, such as at least 18 g/L, such as at least 19 g/L, such as at least 20 g/L, such as at least 25 g/L, such as at least 30 g/L, such as at least 35 g/L, such as at least 40 g/L, such as at least 45 g/L, such as at least 50 g/L, or more.

Also provided herein is a method for increasing the purity of a compound selected from a a desaturated fatty alcohol, a desaturated fatty acid and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:

- a. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- b. expressing in said cell an Ncb5or, thereby increasing the production of said compound compared to the production from a cell not expressing said Ncb5or in the same conditions;

wherein the purity of said compound is the ratio or percentage of said compound in relation to all compounds within the same compound group produced by the cell, such as the percentage of said desaturated fatty alcohol in relation to all desaturated fatty alcohols produced by the cell, such as the percentage of desaturated fatty acid in

relation to all fatty acids produced by the cell, and/or such as the percentage of desaturated fatty acyl-CoA in relation to all fatty acyl-CoA produced by the cell.

Description of figures

5 **Figure 1.** A) Schematic to visualize the domain prediction for classic cytochrome B5, cytochrome B5 reductase and Ncb5or. B) Amino acid alignment and domain prediction of multiple Ncb5ors and classic cytochrome B5 and cytochrome B5 reductase. Domains were predicted using the Batch CD-search tool (<https://www.ncbi.nlm.nih.gov/Structure/bwrpsb/bwrpsb.cgi>).

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Figure 2. Amino acid alignment of predicted cytochrome B5 domains from different Ncb5ors and classic cytochrome B5 proteins; DmCytB5, *Drosophila melanogaster* cytochrome B5 (Uniprot ID Q9V4N3); HsCytB5typeB, *Homo sapiens* cytochrome B5 (Uniprot ID O43169); MaCytB5, *Mortierella alpina* cytochrome B5 (NCBI ID Q9Y706.1); Remaining sequences can be found in the sequence list.

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Detailed description

Definitions

Biopesticide: the term 'biopesticide' is a contraction of 'biological pesticide' and refers to several types of pest management intervention: through predatory, parasitic, or chemical relationships. In the EU, biopesticides have been defined as "a form of pesticide based on micro-organisms or natural products". In the US, they are defined by the EPA as "including naturally occurring substances that control pests (biochemical pesticides), microorganisms that control pests (microbial pesticides), and pesticidal substances produced by plants containing added genetic material (plant-incorporated protectants) or PIPs". The present invention relates more particularly to biopesticides comprising natural products or naturally occurring substances. They are typically created by growing and concentrating naturally occurring organisms and/or their metabolites including bacteria and other microbes, fungi, nematodes, proteins, etc.

20 They are often considered to be important components of integrated pest management (IPM) programmes, and have received much practical attention as substitutes to synthetic chemical plant protection products (PPPs). The Manual of Biocontrol Agents (2009: formerly the Biopesticide Manual) gives a review of the available biological insecticide (and other biology-based control) products.

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- Cloud concentration: the term will herein be used to refer to the concentration of a surfactant, in particular non-ionic, or a glycol solution, in a solution above which, at a given temperature, a mixture of said surfactant and said solution starts to phase-separate, and two phases appear, thus becoming cloudy. For example, the cloud concentration of a surfactant in an aqueous solution at a given temperature is the minimal concentration of said surfactant which, when mixed with the aqueous solution, gives rise to two phases. The cloud concentration can be obtained from the manufacturer of the surfactant, or it may be determined experimentally, by making a dosage curve and determining the concentration at which the mixture phase separates.
- Cloud point: The cloud point of a surfactant, in particular non-ionic, or a glycol solution, in a solution, for example an aqueous solution, is the temperature at which a mixture of said surfactant and said solution, for example said aqueous solution, starts to phase-separate, and two phases appear, thus becoming cloudy. This behavior is characteristic of non-ionic surfactants containing polyoxyethylene chains, which exhibit reverse solubility versus temperature behavior in water and therefore "cloud out" at some point as the temperature is raised. Glycols demonstrating this behavior are known as "cloud-point glycols". The cloud point is affected by salinity, being generally lower in more saline fluids.
- Desaturated: the term "desaturated" will be herein used interchangeably with the term "unsaturated" and refers to a compound containing one or more double or triple carbon-carbon bonds.
- Derived from: the term when referring to a polypeptide or a polynucleotide derived from an organism means that said polypeptide or polynucleotide is native to said organism, i.e. that it is naturally found in said organism.
- Ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agent: the term refers to a group of polyethoxylated, non-ionic surfactants which comprise or mainly consist of ethoxylated and propoxylated alcohols in C₁₆-C₁₈, for example CAS number 68002-96-0, also termed C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate or C₁₆-C₁₈ alcohols ethoxylated propoxylated polymer.

Extractant: the term "extractant" as used herein refers to a non-ionic surfactant such as an antifoaming agent which facilitates recovery of hydrophobic compounds produced in a fermentation, in particular a polyethoxylated surfactant selected from: a polyethylene polypropylene glycol, a mixture of polyether dispersions, an antifoaming agent
5 comprising polyethylene glycol monostearate such as simethicone and ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agents and combinations thereof.

Fatty acid: the term "fatty acid" refers to a carboxylic acid having a long aliphatic chain, i.e. an aliphatic chain between 4 and 28 carbon atoms, such as 4, 5, 6, 7, 8, 9, 10, 11,
10 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28 carbon atoms. Most naturally occurring fatty acids are unbranched. They can be saturated, or desaturated.

Fatty alcohol acetate: the term refers to an acetate having a fatty carbon chain, i.e. an aliphatic chain between 4 and 28 carbon atoms, such as 4, 5, 6, 7, 8, 9, 10, 11, 12, 13,
15 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28 carbon atoms. Fatty acyl acetates can be saturated or desaturated.

Fatty acyl-CoA: the term will herein be used interchangeably with "fatty acyl-CoA ester", and refers to compounds of general formula R-CO-SCoA, where R is a fatty
20 carbon chain having a carbon chain length of 4 to 28 carbon atoms, such as 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28 carbon atoms. The fatty carbon chain is joined to the -SH group of coenzyme A by a thioester bond. Fatty acyl-CoAs can be saturated or desaturated, depending on whether the fatty acid which it is derived from is saturated or desaturated.

25 Fatty alcohol: the term "fatty alcohol" refers herein to an alcohol derived from a fatty acyl-CoA, having a carbon chain length of 4 to 28 carbon atoms, such as 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28 carbon atoms. Fatty alcohols can be saturated or desaturated.

30 Fatty aldehyde: the term refers herein to an aldehyde derived from a fatty acyl-CoA, having a carbon chain length of 4 to 28 carbon atoms, such as 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28 carbon atoms. Fatty aldehydes can be saturated or desaturated.

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Functional variant: the term refers herein to functional variants of an enzyme, which retain at least some of the activity of the parent enzyme. Thus, a functional variant of an acyl-CoA oxidase, a desaturase, an alcohol-forming fatty acyl-CoA reductase, an alcohol dehydrogenase, an aldehyde-forming fatty acyl-CoA reductase, an acetyltransferase, or an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) can catalyse the same conversion as the acyl-CoA oxidase, the desaturase, the alcohol-forming fatty acyl-CoA reductase, the alcohol dehydrogenase, the aldehyde-forming fatty acyl-CoA reductase, or the acetyltransferase, respectively, from which they are derived, although the efficiency of reaction may be different, e.g. the efficiency is decreased or increased compared to the parent enzyme or the substrate specificity is modified.

Heterologous: the term "heterologous" when referring to a polypeptide, such as a protein or an enzyme, or to a polynucleotide, shall herein be construed to refer to a polypeptide or a polynucleotide which is not naturally present in a wild type cell. For example, the term "heterologous $\Delta 9$ desaturase" when applied to *Saccharomyces cerevisiae* refers to a $\Delta 9$ desaturase which is not naturally present in a wild type *S. cerevisiae* cell, e.g. a $\Delta 9$ desaturase derived from *Drosophila melanogaster*.

Identity / homology: the terms identity and homology, with respect to a polynucleotide (or polypeptide), are defined herein as the percentage of nucleic acids (or amino acids) in the candidate sequence that are identical or homologous, respectively, to the residues of a corresponding native nucleic acids (or amino acids), after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity / similarity / homology, and considering any conservative substitutions according to the NCIUB rules (<http://www.chem.qmul.ac.uk/iubmb/misc/naseq.html>; NC-IUB, Eur J Biochem (1985)) as part of the sequence identity. Neither 5' or 3' extensions nor insertions (for nucleic acids) or N' or C' extensions nor insertions (for polypeptides) result in a reduction of identity, similarity or homology. Methods and computer programs for the alignments are well known in the art. Generally, a given homology between two sequences implies that the identity between these sequences is at least equal to the homology; for example, if two sequences are 70% homologous to one another, they cannot be less than 70% identical to one another – but could be sharing 80% identity.

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Increased activity: the term "increased activity" may herein refer to an increase in activity of a given peptide, such as a protein or an enzyme. The increase in activity can be measured using methods known in the art, such as for example using enzyme assays to measure the increase in activity of an enzyme. In some cases, the increase

5 in activity results in higher production of the compound or compounds which the enzyme is generating, i.e. the product. Thus, increased activity of an enzyme may be measured by measuring the amount, such as the concentration, of said product. If an enzyme has increased activity, the concentration of product will be higher compared the concentration of product generated in similar or identical conditions by the same

10 enzyme which does not have increased activity, e.g. the parent enzyme or unmodified enzyme. If the enzyme with increased activity is expressed inside a cell, the product can be measured as the product titer, i.e. the amount of product said cell has produced, and can be compared to the titer or amount of the same product obtained in similar or identical conditions from a cell expressing the parent or unmodified enzyme

15 but otherwise having an identical or similar genotype as the cell expressing the enzyme with increased activity.

Native: the term "native" when referring to a polypeptide, such as a protein or an enzyme, or to a polynucleotide, shall herein be construed to refer to a polypeptide or a

20 polynucleotide which is naturally present in a wild type cell.

Pest: as used herein, the term 'pest' shall refer to an organism, in particular an animal, detrimental to humans or human concerns, in particular in the context of agriculture or livestock production. A pest is any living organism which is invasive or prolific,

25 detrimental, troublesome, noxious, destructive, a nuisance to either plants or animals, human or human concerns, livestock, human structures, wild ecosystems etc. The term often overlaps with the related terms vermin, weed, plant and animal parasites and pathogens. It is possible for an organism to be a pest in one setting but beneficial, domesticated or acceptable in another.

30 Pheromone: pheromones are naturally occurring compounds. Lepidopteran pheromones are designated by an unbranched aliphatic chain (between 9 and 18 carbons, such as 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18 carbon atoms) ending in an alcohol, aldehyde or acetate functional group and containing up to 3 double bonds in

35 the aliphatic backbone. Thus, desaturated fatty alcohols, desaturated fatty aldehydes

and desaturated fatty alcohol acetates are typically comprised in pheromones. Pheromone compositions may be produced chemically or biochemically, for example as described herein. Pheromones thus comprise desaturated fatty alcohols, desaturated fatty aldehydes and/or desaturated fatty alcohol acetates, such as can be
5 obtained by the methods and cells described herein.

Purity: the term "purity" as used herein refers to the ratio or percentage of a compound in relation to all compounds within the same compound group produced by the cell. For example, the purity of a specific desaturated fatty alcohol is the percentage of said
10 desaturated fatty alcohol in relation to all desaturated fatty alcohols produced by the cell; the purity of a fatty acid is the percentage of said fatty acid in relation to all fatty acids produced by the cell; and the purity of a desaturated fatty-acyl CoA is the percentage of said desaturated fatty acyl-CoA in relation to all fatty acyl-CoA produced by the cell.

15 Reduced activity: the term "reduced activity" may herein refer to a total or a partial loss of activity of a given peptide, such as a protein or an enzyme. In some cases, peptides are encoded by essential genes, which cannot be deleted. In these cases, activity of the peptide can be reduced by methods known in the art, such as down-regulation of
20 transcription or translation, inhibition of the peptide. In other cases, the peptide is encoded by a non-essential gene, and the activity may be reduced or it may be completely lost, e.g. as a consequence of a deletion of the gene encoding the peptide. In order to reduce, whether partially or totally, the activity of a given peptide, methods known in the art include not only mutations in the genes encoding said peptide, but
25 also mutation of genes encoding regulatory factors involved in transcription or translation of the gene encoding said peptide, e.g. mutation of transcription factor genes or of transcription repressor genes resulting in increased or decreased expression of said transcription factors or repressors, which in turn reduce transcription levels from the gene encoding the peptide; truncation or mutation of the native
30 promoter of the gene, for example to remove transcription factor binding sites or to render them inaccessible to said transcription factors; replacement of the native promoter with a weaker promoter, leading to reduced transcription of the coding sequence encoding the peptide; truncation or mutation of the native terminator of the gene, or replacement of the native terminator of the gene with another terminator
35 sequence; mutation of the Kozak sequence. Other methods involve regulation at the

RNA level, and include RNA interference systems such as Dicer or Argonaute, RNA silencing methods, introduction of CRISPR/Cas systems resulting in targeted RNA degradation. Regulation at the protein level is also envisaged, e.g. by using inhibitors or protein degradation sequences. The listed methods may be inducible, i.e. they may
5 be activated in a transient manner as known in the art.

Saturated: the term "saturated" refers to a compound which is devoid of double or triple carbon-carbon bonds.

10 Specificity: the specificity of an enzyme towards a given substrate is the preference exhibited by this enzyme to catalyse a reaction starting from said substrate. In the present disclosure, a desaturase and/or a fatty acyl-CoA reductase having a higher specificity towards tetradecanoyl-CoA (myristoyl-CoA) than towards hexadecanoyl-CoA (palmitoyl-CoA) preferably catalyse a reaction with tetradecanoyl-CoA than with
15 hexadecanoyl-CoA as a substrate. Methods to determine the specificity of a desaturase or a fatty acyl-CoA reductase are known in the art. For example, specificity of a given desaturase in a given cell expressing it can be determined by incubating said cell in a solution comprising methyl myristate for up to 48 hours, followed by extraction and esterification of the products with methanol. The profiles of the resulting fatty acid
20 methyl esters can then be determined by GC-MS. Desaturases with higher specificity towards myristoyl-CoA and low specificity towards palmitoyl-CoA, for example, will result in higher concentration of (Z)9-C14:Me than (Z)9-C16:Me. For example, specificity of a given reductase in a given cell can be determined by incubating cells that express said reductase in a solution comprising methyl ester of (Z)9-myristate for
25 up to 48 hours, followed by extraction and analysis of the resulting fatty alcohols by GC-MS. Reductases with higher specificity towards (Z)9-C14:CoA and low specificity towards (Z)9-C16:CoA will result in higher concentration of (Z)9-C14:OH than (Z)9-C16:OH.

30 Titer: the titer of a compound refers herein to the produced concentration of a compound. When the compound is produced by a cell, the term refers to the total concentration produced by the cell, i.e. the total amount of the compound divided by the volume of the culture medium. This means that, particularly for volatile compounds, the titer includes the portion of the compound which may have evaporated from the

culture medium, and it is thus determined by collecting the produced compound from the fermentation broth and from potential off-gas from the fermenter.

5 The present inventors have discovered that NAD(P)H cytochrome b5 oxidoreductases (Ncb5ors) are enzymes which increase the activity of other enzymes, in particular membrane-bound enzymes localised in the cell membrane. Ncb5ors can thus, when expressed in cells engineered to produce compounds such as desaturated and saturated fatty alcohols, desaturated and saturated fatty aldehydes, and desaturated and saturated fatty alcohol acetates, the production of which relies on such membrane-bound enzymes, significantly improve production of these compounds. In other words, 10 Ncb5ors significantly increase the activity of certain enzymes, such as of fatty acyl desaturases and of reductases such as fatty acyl-CoA reductases and cytochrome P450.

15 Herein are disclosed cells capable of producing compounds such as the ones listed above. Said cells express: a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and a heterologous Ncb5or; whereby the cells are capable of producing the compound with a higher titer compared to a cell expressing the first group of enzymes but no 20 heterologous Ncb5or when cultivated in the same conditions. Preferably, the first enzyme or group of enzymes are heterologous enzymes, i.e. are not naturally expressed in the cell.

25 In one embodiment, the first enzyme or group of enzymes may comprise or consist of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA, whereby the cell is capable of producing a desaturated fatty acyl-CoA with a higher titer compared to a cell expressing said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.

30 In another embodiment, the first enzyme or group of enzymes comprises or consists of one or more fatty acyl reductase (FAR) capable of converting a saturated or desaturated fatty acyl-CoA to a saturated or desaturated fatty alcohol, respectively, whereby the cell is capable of producing a saturated or desaturated fatty alcohol with a

higher titer compared to a cell expressing said one or more FAR but no heterologous Ncb5or when cultivated in the same conditions.

5 In yet another embodiment, the first enzyme or group of enzymes comprises or consists of one or more fatty acyl reductase (FAR) and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol, whereby the cell is capable of producing a desaturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR and said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.

10 The cell may further express an acetyltransferase, whereby said cell is capable of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively, whereby the cell is capable of producing a desaturated or a saturated fatty alcohol acetate with a higher titer compared to a cell
15 expressing the first group of enzymes and the acetyltransferase but no heterologous Ncb5or when cultivated in the same conditions.

20 Preferably, the first enzyme or group of enzymes are native to insect species. In some embodiments, the first enzyme or group of enzymes are heterologous desaturases and reductases. Such cells produce desaturated fatty alcohols, saturated fatty alcohols, and desaturated fatty alcohol acetates, i.e. produce pheromone compounds with a higher titer compared to cells expressing the same heterologous desaturase and reductase but not expressing a heterologous Ncb5or.

25 The desaturase introduces at least one double bond in an acyl-CoA, which is then converted into the corresponding alcohol by the action of the reductase. This desaturated fatty alcohol can then further be converted into a desaturated fatty alcohol acetate and/or a desaturated fatty aldehyde, as detailed herein.

30 *Desaturase*

In the present invention, the terms 'fatty acyl-CoA desaturase', 'desaturase', 'fatty acyl desaturase' and 'FAD' will be used interchangeably. The term generally refers to an enzyme capable of introducing at least one double bond in E/Z confirmations in an acyl-CoA having a chain length of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or

22 carbon atoms. The double bond may be introduced in any position. For example, a desaturase introducing a double bond in position 9 is termed $\Delta 9$ desaturase.

Desaturases catalyse the reaction:

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Fatty acyl-CoA + 2 ferrocytochrome b5 + O(2) + 2 H(+) $\rightleftharpoons$ desaturated fatty acyl-CoA + 2 ferricytochrome b5 + 2 H(2)O

The heterologous desaturase may be native to any type of organism. In some
 10 embodiments, the heterologous desaturase is native to a plant, such as such as *Ricinus communis* or *Pelargonium hortorum*. In another embodiment, the heterologous desaturase is native to an insect, such as of the *Diptera*, the *Coleoptera*, or the *Lepidoptera* order, such as of the genus *Agrotis*, *Antheraea*, *Argyrotaenia*, *Amyelois*, *Bombus*, *Bombyx*, *Cadra*, *Chauliognathus*, *Chilo*, *Choristoneura*, *Cydia*, *Dendrophilus*,
 15 *Diatraea*, *Drosophila*, *Ephestia*, *Epiphyas*, *Grapholita*, *Helicoverpa*, *Lampronia*, *Lobesia*, *Manducta*, *Ostrinia*, *Pectinophora*, *Plodia*, *Plutella*, *Thalassiosira*, *Thaumatopoea*, *Tribolium*, *Trichoplusia*, *Spodoptera* or *Yponomeuta*, such as *Agrotis segetum*, *Antheraea pernyi*, *Argyrotaenia velutiana*, *Amyelois transitella*, *Bombus lapidarius*, *Bombyx mori*, *Cadra cautella*, *Chauliognathus lugubris*, *Chilo suppressalis*, *Choristoneura parallela*, *Choristoneura rosaceana*, *Cydia pomonella*, *Dendrophilus punctatus*, *Diatraea saccharalis*, *Drosophila ananassae*, *Drosophila melanogaster*, *Drosophila virilis*, *Drosophila yakuba*, *Ephestia elutella*, *Ephestia kuehniella*, *Epiphyas postvittana*, *Grapholita molesta*, *Helicoverpa assulta*, *Helicoverpa zea*, *Lampronia capitella*, *Lobesia botrana*, *Manducta sexta*, *Ostrinia furnacalis*,
 20 *Ostrinia nubilalis*, *Pectinophora gossypiella*, *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*, *Spodoptera littoralis*, *Spodoptera litura*, *Thalassiosira pseudonana*, *Thaumatopoea pityocampa*, *Tribolium castaneum*, *Trichoplusia ni*, or *Yponomeuta padella*.

30 In some embodiments, the cell is capable of expressing a first enzyme or group of enzymes which comprises or consists of a desaturase. In one embodiment, the cell is capable of expressing at least one heterologous $\Delta 5$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 6$ desaturase. In another embodiment, the cell is capable of expressing at least one
 35 heterologous $\Delta 7$ desaturase. In another embodiment, the cell is capable of expressing

at least one heterologous $\Delta 8$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 9$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 10$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 11$

5 desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 12$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 13$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 14$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 15$ desaturase. In another

10 embodiment, the cell is capable of expressing at least one heterologous $\Delta 16$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 17$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 18$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 19$ desaturase. In another embodiment, the

15 cell is capable of expressing at least one heterologous $\Delta 20$ desaturase. In another embodiment, the cell is capable of expressing at least one heterologous $\Delta 21$ desaturase. In preferred embodiments, the desaturase is a $\Delta 9$ desaturase or a $\Delta 11$ desaturase.

20 The gene encoding the heterologous desaturase may be codon-optimized for the cell, as is known in the art. Methods to determine whether the desaturase is expressed in the cell are known to the person of skill in the art, and include for instance detection of a given product from a given substrate, as detailed herein above and as illustrated in the examples below.

25 The skilled person will know, depending on which desaturated fatty alcohol is desired, which kind of desaturase to use. For example, for the production of a fatty alcohol desaturated in position 11, a $\Delta 11$ desaturase is preferably used. If a fatty alcohol desaturated in position 9 is desired, a $\Delta 9$ desaturase may be used, such as a $\Delta 9$

30 desaturase having at least 60% identity to a *Drosophila* desaturase such as a *Drosophila* $\Delta 9$ desaturase, for example the $\Delta 9$ desaturase from *Drosophila melanogaster* as set forth in SEQ ID NO: 14 or a $\Delta 9$ desaturase having at least 60% identity thereto, or to a *Spodoptera* desaturase such as a *Spodoptera* $\Delta 9$ desaturase, for example the $\Delta 9$ desaturase from *Spodoptera litura* as set forth in SEQ ID NO: 33 or

35 a $\Delta 9$ desaturase having at least 60% identity thereto.

In some embodiments, the desaturase is a desaturase selected from the group of desaturases set forth in SEQ ID NOs: 1 to 38 and SEQ ID NOs: 126 to 139, or variants thereof having at least 60% identity thereto, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99%, such as 100% identity a desaturase selected from the group of desaturases set forth in SEQ ID NOs: 1 to 38.

In one embodiment, the heterologous desaturase is an *Agrotis* desaturase. In one embodiment, the desaturase is an *Agrotis segetum* desaturase, such as the desaturase as set forth in SEQ ID NO: 1 (Desat19). In some embodiments, the desaturase is a variant of an *Agrotis* desaturase, a variant of an *Agrotis segetum* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 1 (Desat19), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is an *Amyelois* desaturase. In one embodiment, the desaturase is an *Amyelois transitella* desaturase, such as the desaturase as set forth in SEQ ID NO: 3 (Desat17), as set forth in SEQ ID NO: 2 (Desat16) or as set forth in SEQ ID NO: 4 (Desat18). In some embodiments, the desaturase is a variant of an *Amyelois* desaturase, a variant of an *Amyelois transitella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 3 (Desat17), as set forth in SEQ ID NO: 2 (Desat16) or as set forth in SEQ ID NO: 4 (Desat18), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is an *Antheraea* desaturase. In one embodiment, the desaturase is an *Antheraea pernyi* desaturase, such as the desaturase as set forth in SEQ ID NO: 126 (Desat72). In some embodiments, the

desaturase is a variant of an *Antheraea* desaturase, a variant of an *Antheraea pernyi* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 126 (Desat72), having at least 60% identity thereto.

5 In one embodiment, the heterologous desaturase is an *Argyrotaenia* desaturase. In one embodiment, the desaturase is an *Argyrotaenia velutinana* desaturase, such as the desaturase as set forth in SEQ ID NO: 127 (Desat76). In some embodiments, the desaturase is a variant of an *Argyrotaenia* desaturase, a variant of an *Argyrotaenia velutinana* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 127
10 (Desat76), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Bombus* desaturase. In one embodiment, the desaturase is a *Bombus lapidarius* desaturase, such as the desaturase as set forth in SEQ ID NO: 128 (Desat75). In some embodiments, the
15 desaturase is a variant of a *Bombus* desaturase, a variant of a *Bombus lapidarius* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 128 (Desat75), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Bombyx* desaturase. In one embodiment, the desaturase is a *Bombyx mori* desaturase, such as the desaturase as set forth in SEQ ID NO: 129 (Desat78). In some embodiments, the desaturase is a variant of a *Bombyx mori* desaturase, a variant of a *Bombyx mori* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 129 (Desat78), having at least
20 60% identity thereto.

25 In one embodiment, the heterologous desaturase is a *Cadra* desaturase. In one embodiment, the desaturase is a *Cadra cautella* desaturase, such as the desaturase as set forth in SEQ ID NO: 134 (Desat70). In some embodiments, the desaturase is a variant of a *Cadra* desaturase, a variant of a *Cadra cautella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 134 (Desat70), having at least 60% identity thereto.
30

In one embodiment, the heterologous desaturase is a *Chauliognathus* desaturase. In one embodiment, the desaturase is a *Chauliognathus lugubris* desaturase, such as the desaturase as set forth in SEQ ID NO: 5 (Desat25). In some embodiments, the
35

desaturase is a variant of a *Chauliognathus* desaturase, a variant of a *Chauliognathus lugubris* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 5 (Desat25), having at least 60% identity thereto.

5 In one embodiment, the heterologous desaturase is a *Chilo* desaturase. In one embodiment, the desaturase is a *Chilo suppressalis* desaturase, such as the desaturase as set forth in SEQ ID NO: 6 (Desat47) or SEQ ID NO: 130 (Desat44). In some embodiments, the desaturase is a variant of a *Chilo* desaturase, a variant of a *Chilo suppressalis* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 6
10 (Desat47) or SEQ ID NO: 130 (Desat44), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Choristoneura* desaturase. In one embodiment, the desaturase is a *Choristoneura parallela* desaturase, such as the desaturase as set forth in SEQ ID NO: 7 (Desat36), or a *Choristoneura rosaceana*
15 desaturase, such as the desaturase as set forth in SEQ ID NO: 8 (Desat35). In some embodiments, the desaturase is a variant of a *Choristoneura* desaturase, a variant of a *Choristoneura parallela* desaturase, a *Choristoneura rosaceana* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 7 (Desat36), of the desaturase as set forth in SEQ ID NO: 8 (Desat35), having at least 60% identity thereto.

20 In one embodiment, the heterologous desaturase is a *Cydia* desaturase. In one embodiment, the desaturase is a *Cydia pomonella* desaturase, such as the desaturase as set forth in SEQ ID NO: 9 (Desat4), the desaturase as set forth in SEQ ID NO: 10 (Desat2) or the desaturase as set forth in SEQ ID NO: 11 (Desat1). In some
25 embodiments, the desaturase is a variant of a *Cydia* desaturase, a variant of a *Cydia pomonella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 9 (Desat4), the desaturase as set forth in SEQ ID NO: 10 (Desat2) or the desaturase as set forth in SEQ ID NO: 11 (Desat1), having at least 60% identity thereto.

30 In one embodiment, the heterologous desaturase is a *Dendrolimus* desaturase. In one embodiment, the desaturase is a *Dendrolimus punctatus* desaturase, such as the desaturase as set forth in SEQ ID NO: 12 (Desat40). In some embodiments, the desaturase is a variant of a *Dendrolimus* desaturase, a variant of a *Dendrolimus punctatus* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 12
35 (Desat40), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Diatraea* Z11 desaturase. In one embodiment, the desaturase is a *Diatraea saccharalis* Z11 desaturase, such as the Z11 desaturase as set forth in SEQ ID NO: 132 (Desat63). In some embodiments, the desaturase is a variant of a *Diatraea* Z11 desaturase, a variant of a *Diatraea saccharalis* Z11 desaturase or a variant of the Z11 desaturase as set forth in SEQ ID NO: 132 (Desat63), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Drosophila* desaturase. In one embodiment, the desaturase is a *Drosophila virilis* desaturase, for example such as Desat61 as set forth in SEQ ID NO: 15. In one embodiment, the desaturase is a *Drosophila ananassae* desaturase, for example such as the desaturase set forth in SEQ ID NO: 131 (Desat60). In one embodiment, the desaturase is a *Drosophila melanogaster* desaturase, for example such as the desaturase set forth in SEQ ID NO: 14 (Desat24). In one embodiment, the desaturase is a *Drosophila grimshawi* desaturase, for example such as the desaturase set forth in SEQ ID NO: 13 (Desat59). In one embodiment, the desaturase is a *Drosophila yakuba* desaturase, for example such as the desaturase set forth in SEQ ID NO: 133 (Desat56). In some embodiments, the desaturase is a variant of a *Drosophila* desaturase, a variant of a *Drosophila ananassae* desaturase, a variant of a *Drosophila virilis* desaturase, a variant of a *Drosophila melanogaster* desaturase, a variant of a *Drosophila grimshawi* desaturase, a variant of a *Drosophila yakuba* desaturase, such as a variant of the desaturase as set forth in SEQ ID NO: 131 (Desat60), of the desaturase as set forth in SEQ ID NO: 14 (Desat24), of the desaturase as set forth in SEQ ID NO: 15 (Desat61) or of the desaturase as set forth in SEQ ID NO: 13 (Desat59), of the desaturase as set forth in SEQ ID NO: 133 (Desat56), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is an *Epiphyas* desaturase. In one embodiment, the desaturase is an *Epiphyas postvittana* desaturase, such as the desaturase as set forth in SEQ ID NO: 16 (Desat33). In some embodiments, the desaturase is a variant of an *Epiphyas* desaturase, a variant of an *Epiphyas postvittana* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 16 (Desat33), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Grapholita* desaturase. In one embodiment, the desaturase is a *Grapholita molesta* desaturase, such as the desaturase as set forth in SEQ ID NO: 17 (Desat31) or as set forth in SEQ ID NO: 18 (Desat55). In some embodiments, the desaturase is a variant of a *Grapholita* desaturase, a variant of a *Grapholita molesta* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 17 (Desat31) or as set forth in SEQ ID NO: 18 (Desat55), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Helicoverpa* desaturase. In one embodiment, the desaturase is a *Helicoverpa zea* desaturase, such as Desat51 as set forth in SEQ ID NO: 19. In some embodiments, the desaturase is a variant of a *Helicoverpa* desaturase, a variant of a *Helicoverpa zea* desaturase or a variant of Desat51 as set forth in SEQ ID NO: 19, having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Lobesia* desaturase. In one embodiment, the desaturase is a *Lobesia botrana* desaturase, such as Desat30 (SEQ ID NO: 20), Desat71 (SEQ ID NO: 135) or Desat43 (SEQ ID NO: 21). In some embodiments, the desaturase is a variant of a *Lobesia* desaturase, a variant of a *Lobesia botrana* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 20 (Desat30), as set forth in SEQ ID NO: 135 (Desat71) or as set forth in SEQ ID NO: 21 (Desat43), having at least 60% identity.

In one embodiment, the heterologous desaturase is a *Manducta* desaturase. In one embodiment, the desaturase is a *Manducta sexta* desaturase, such as the desaturase as set forth in SEQ ID NO: 22 (Desat52). In some embodiments, the desaturase is a variant of an *Manducta* desaturase, a variant of an *Manducta sexta* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 22 (Desat52), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is an *Ostrinia* desaturase. In one embodiment, the desaturase is an *Ostrinia nubilalis* desaturase, such as the desaturase as set forth in SEQ ID NO: 23 (Desat32). In one embodiment, the desaturase is an *Ostrinia furnacalis* desaturase, such as the desaturase as set forth in SEQ ID NO: 136 (Desat77). In some embodiments, the desaturase is a variant of an *Ostrinia* desaturase, a variant of an *Ostrinia nubilalis* desaturase, a variant of an

Ostrinia furnacalis desaturase, or a variant of the desaturase as set forth in SEQ ID NO: 23 (Desat32) or as set forth in SEQ ID NO: 136 (Desat77), having at least 60% identity thereto.

5 In one embodiment, the heterologous desaturase is a *Pectinophora* desaturase. In one embodiment, the desaturase is a *Pectinophora gossypiella* desaturase, such as the desaturase as set forth in SEQ ID NO: 24 (Desat48). In some embodiments, the desaturase is a variant of a *Pectinophora* desaturase, a variant of a *Pectinophora gossypiella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 24
10 (Desat48), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Pelargonium* desaturase. In one embodiment, the desaturase is a *Pelargonium hortorum* desaturase, such as the desaturase as set forth in SEQ ID NO: 25 (Desat22). In some embodiments, the
15 desaturase is a variant of a *Pelargonium* desaturase, a variant of a *Pelargonium hortorum* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 25 (Desat22) having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Plodia* desaturase. In one
20 embodiment, the desaturase is a *Plodia interpunctella* desaturase, such as the desaturase as set forth in SEQ ID NO: 137 (Desat65). In some embodiments, the desaturase is a variant of a *Plodia* desaturase, a variant of a *Plodia interpunctella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 137 (Desat65) having at least 60% identity thereto.

25 In one embodiment, the heterologous desaturase is a *Plutella* desaturase. In one embodiment, the desaturase is a *Plutella xylostella* desaturase, such as the desaturase as set forth in SEQ ID NO: 26 (Desat45). In some embodiments, the desaturase is a variant of a *Plutella* desaturase, a variant of a *Plutella xylostella* desaturase or a variant
30 of the desaturase as set forth in SEQ ID NO: 26 (Desat45) having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is a *Ricinus* desaturase. In one
embodiment, the desaturase is a *Ricinus communis* desaturase, such as Desat23 as
35 set forth in SEQ ID NO: 27. In some embodiments, the desaturase is a variant of a

Ricinus desaturase, a variant of a *Ricinus communis* desaturase or a variant of Desat23 as set forth in SEQ ID NO: 27, having at least 60% identity thereto.

5 In one embodiment, the heterologous desaturase is a *Saccharomyces* desaturase. In one embodiment, the desaturase is a *Saccharomyces cerevisiae* desaturase, such as the desaturase as set forth in SEQ ID NO: 28 (Desat42). In some embodiments, the desaturase is a variant of a *Saccharomyces* desaturase, a variant of a *Saccharomyces cerevisiae* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 28 (Desat42), having at least 60% identity thereto.

10 In one embodiment, the heterologous desaturase is a *Spodoptera* desaturase. In one embodiment, the desaturase is a *Spodoptera littoralis* desaturase, such as the desaturase as set forth in SEQ ID NO: 31 (Desat20), or a *Spodoptera litura* desaturase, such as the desaturase as set forth in SEQ ID NO: 32 (Desat38) or as set
15 forth in SEQ ID NO: 33 (Desat26), or a *Spodoptera exigua* desaturase, such as the desaturase as set forth in SEQ ID NO: 29 (Desat37). In some embodiments, the desaturase is a variant of a *Spodoptera* desaturase, a variant of a *Spodoptera littoralis* desaturase, a variant of a *Spodoptera litura* desaturase, a variant of a *Spodoptera exigua* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 31
20 (Desat20), as set forth in SEQ ID NO: 32 (Desat38), as set forth in SEQ ID NO: 33 (Desat26), or as set forth in SEQ ID NO: 29 (Desat37), having at least 60% identity thereto.

25 In one embodiment, the heterologous desaturase is a *Thaumetopoea* desaturase. In one embodiment, the desaturase is a *Thaumetopoea pityocampa* desaturase, such as the desaturase as set forth in SEQ ID NO: 34 (Desat34). In some embodiments, the desaturase is a variant of a *Thaumetopoea* desaturase, a variant of a *Thaumetopoea pityocampa* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 34 (Desat34), having at least 60% identity thereto.

30 In one embodiment, the heterologous desaturase is a *Tribolium* desaturase. In one embodiment, the desaturase is a *Tribolium castaneum* desaturase, such as the desaturase as set forth in SEQ ID NO: 35 (Desat28), as set forth in SEQ ID NO: 138 (Desat27), or as set forth in SEQ ID NO: 36 (Desat29). In some embodiments, the
35 desaturase is a variant of a *Tribolium* desaturase, a variant of a *Tribolium castaneum*

desaturase or a variant of the desaturase as set forth in SEQ ID NO: 35 (Desat28), as set forth in SEQ ID NO: 138 (Desat27) or as set forth in SEQ ID NO: 36 (Desat29), having at least 60% identity thereto.

5 In one embodiment, the heterologous desaturase is a *Trichoplusia* desaturase. In one embodiment, the desaturase is a *Trichoplusia ni* desaturase, such as the desaturase as set forth in SEQ ID NO: 37 (Desat21). In some embodiments, the desaturase is a variant of a *Trichoplusia* desaturase, a variant of a *Trichoplusia ni* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 37 (Desat21), having at least 60%
10 identity thereto.

In one embodiment, the heterologous desaturase is a *Yarrowia* desaturase. In one embodiment, the desaturase is a *Yarrowia lipolytica* desaturase, such as the desaturase as set forth in SEQ ID NO: 38 (Desat69). In some embodiments, the
15 desaturase is a variant of a *Yarrowia* desaturase, a variant of a *Yarrowia lipolytica* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 38 (Desat69), having at least 60% identity thereto.

In one embodiment, the heterologous desaturase is an *Yponomeuta* desaturase. In one embodiment, the desaturase is an *Yponomeuta padella* desaturase, such as the desaturase as set forth in SEQ ID NO: 139 (Desat73). In some embodiments, the desaturase is a variant of an *Yponomeuta* desaturase, a variant of an *Yponomeuta padella* desaturase or a variant of the desaturase as set forth in SEQ ID NO: 139 (Desat73), having at least 60% identity thereto.

25 It will be understood that a variant desaturase having at least 60% identity to a given desaturase as above may have at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least
30 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as
35 at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such

as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to the desaturase, or more.

5 Nucleic acids encoding desaturases

In some embodiments, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to a nucleic acid selected from the group of desaturases set forth in SEQ ID NOs: 39 to 76 and SEQ ID NOs: 140 to 153, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity, such as 100% identity thereto.

In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Agrotis segetum* desaturase, as set forth in SEQ ID NO: 39. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Amyelois transitella* desaturase, as set forth in SEQ ID NO: 40, SEQ ID NO: 41 or SEQ ID NO: 42. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Antheraea pernyi* desaturase, as set forth in SEQ ID NO: 140. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Argyrotaenia velutinana* desaturase, as set forth in SEQ ID NO: 141. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Bombus lapidarius* desaturase, as set forth in SEQ ID NO: 142. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid

encoding a *Bombyx mori* desaturase, as set forth in SEQ ID NO: 143. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Cadra cautella* desaturase, as set forth in SEQ ID NO: 148. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Chauliognathus lugubris* desaturase, as set forth in SEQ ID NO: 43. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Chilo suppressalis* desaturase, as set forth in SEQ ID NO: 44 or SEQ ID NO: 144. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Choristoneura parallela* desaturase, as set forth in SEQ ID NO: 45. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Choristoneura rosaceana* desaturase, as set forth in SEQ ID NO: 46. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Cydia pomonella* desaturase, as set forth in SEQ ID NO: 47, in SEQ ID NO: 48 or in SEQ ID NO: 49. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Dendrolimus punctatus* desaturase, as set forth in SEQ ID NO: 50. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Diatraea saccharalis* desaturase, as set forth in SEQ ID NO: 146. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Drosophila virilis* desaturase, as set forth in SEQ ID NO: 53. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Drosophila ananassae* desaturase, as set forth in SEQ ID NO: 145. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Drosophila melanogaster* desaturase, as set forth in SEQ ID NO: 52. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Drosophila yakuba* desaturase, as set forth in SEQ ID NO: 147. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Drosophila grimshawi* desaturase, as set forth in SEQ ID NO: 51. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Epiphyas postvittana* desaturase, as set forth in SEQ ID

NO: 54. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Grapholita molesta* desaturase, as set forth in SEQ ID NO: 55 or SEQ ID NO: 56. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Helicoverpa zea* desaturase, as set forth in SEQ ID NO: 57. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Lobesia botrana* desaturase, as set forth in SEQ ID NO: 58, in SEQ ID NO: 149 or in SEQ ID NO: 59. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Manduca sexta* desaturase, as set forth in SEQ ID NO: 60. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Ostrinia nubilalis* desaturase, as set forth in SEQ ID NO: 61. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding an *Ostrinia furnacalis* desaturase, as set forth in SEQ ID NO: 150. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Pectinophora gossypiella* desaturase, as set forth in SEQ ID NO: 62. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Pelargonium hortorum* desaturase, as set forth in SEQ ID NO: 63. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Plodia interpunctella* desaturase, as set forth in SEQ ID NO: 151. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Plutella xylostella* desaturase, as set forth in SEQ ID NO: 64. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Ricinus communis* desaturase, as set forth in SEQ ID NO: 65. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Saccharomyces cerevisiae* desaturase, as set forth in SEQ ID NO: 66. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Spodoptera exigua* desaturase, as set forth in SEQ ID NO: 67. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Spodoptera littoralis* desaturase, as set forth in SEQ ID NO: 68, or in SEQ ID NO: 69. In one embodiment, the heterologous

desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Spodoptera litura* desaturase, as set forth in SEQ ID NO: 70 or in SEQ ID NO: 71. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Thaumetopoea pityocampa* desaturase, as set forth in SEQ ID NO: 72. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Tribolium castaneum* desaturase, as set forth in SEQ ID NO: 73, in SEQ ID NO: 152 or in SEQ ID NO: 74. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Trichoplusia ni* desaturase, as set forth in SEQ ID NO: 75. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Yarrowia lipolytica* desaturase, as set forth in SEQ ID NO: 76. In one embodiment, the heterologous desaturase is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a *Yponomeuta padella* desaturase, as set forth in SEQ ID NO: 76. Herein, a nucleic acid having at least 60% identity to a given nucleic acid may have at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% to the given nucleic acid, or more.

Co-expression of a plurality of heterologous desaturases

The present cells may express at least one heterologous desaturase. In some embodiments, the cell expresses one heterologous desaturase. It may however be desirable to express several heterologous desaturases, such as at least two heterologous desaturases, which may be identical or different. Alternatively, it may be desirable to express several copies of the nucleic acid encoding the at least one heterologous desaturases, such as at least two copies, at least three copies or more. In

other embodiments, the cell expresses at least two heterologous desaturases, for example three heterologous desaturases.

5 The cell to be modified may express a native desaturase, which may have a negative impact on the production of desaturated fatty alcohol and/or desaturated fatty alcohol acetate. Accordingly, if the cell to be modified expresses such a native desaturase, the organism may preferably be modified so that activity of the native desaturase is reduced or absent.

10 To ensure lack of activity of a native desaturase, methods known in the art can be employed. The gene encoding the native desaturase may be deleted or partly deleted in order to ensure that the native desaturase is not expressed. Alternatively, the gene may be mutated so that the native desaturase is expressed but lacks activity, e.g. by mutation of the catalytic site of the enzyme. Alternatively, translation of mRNA to an
15 active protein may be prevented by methods such as silencing RNA or siRNA. Alternatively, the cell may be incubated in a medium comprising an inhibitor which inhibits activity of the native desaturase. A compound inhibiting transcription of the gene encoding the native desaturase may also be provided so that transcription is inactivated when said compound is present. Other methods are known in the art may
20 be employed.

Inactivation of the native desaturase may thus be permanent or long-term, i.e. the modified cell exhibits reduced or no activity of the native desaturase in a stable manner, or it may be transient, i.e. the modified cell may exhibit activity of the native
25 desaturase for periods of time, but this activity can be suppressed for other periods of time.

Increased C14 specificity

Many desirable pheromone compounds have a carbon chain length of 14. It may thus
30 be of interest to direct the reaction towards the production of C14 compounds. In some embodiments, the cell disclosed herein expresses a desaturase having a higher specificity towards tetradecanoyl-CoA than towards hexadecanoyl-CoA and/or an acyl-CoA reductase having a higher specificity towards desaturated tetradecanoyl-CoA than towards desaturated hexadecanoyl-CoA. In other words, the desaturase is more
35 specific for substrates having a carbon chain length of 14 than for substrates having a

chain length of 16. Examples of yeast cells expressing such desaturases are disclosed in WO 2018/109167.

Expression of such desaturases (and of any of the reductases described herein below) in the cell increases the fraction of total desaturated fatty alcohols having a carbon chain length of 14, particularly compared to the fraction of total desaturated fatty alcohols having a carbon chain length of 16. Desaturases which have the required specificity are in particular desaturases native to *Drosophila*, *Spodoptera*, *Choristoneura* species, such as desaturases native to *Drosophila melanogaster*, *Drosophila grimshawi*, *Drosophila virilis*, *Spodoptera litura*, *Choristoneura parallela* or *Choristoneura rosaceana*, for example as set forth in SEQ ID NOs: 1 to 38, or variants thereof having at least 60% identity thereto.

In some embodiments, the desaturase is selected from the groups consisting of:

- i) a $\Delta 9$ desaturase having at least 60% identity to the $\Delta 9$ desaturase from *Drosophila melanogaster* as set forth in SEQ ID NO: 14;
- ii) a desaturase having at least 60% identity to the $\Delta 9$ desaturase from *Drosophila grimshawi* as set forth in SEQ ID NO: 13;
- iii) a desaturase having at least 60% identity to the $\Delta 9$ desaturase from *Drosophila virilis* as set forth in SEQ ID NO: 15;
- iv) a $\Delta 9$ desaturase having at least 60% identity to the $\Delta 9$ desaturase from *Spodoptera litura* as set forth in SEQ ID NO: 33;
- v) a $\Delta 11$ desaturase having at least 60% identity to the $\Delta 11$ desaturase from *Choristoneura parallela* as set forth in SEQ ID NO: 7;
- vi) a $\Delta 11$ desaturase having at least 60% identity to the $\Delta 11$ desaturase from *Choristoneura rosaceana* as set forth in SEQ ID NO: 8;

and functional variants thereof having at least 60% identity thereto, 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such

as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%,
such as at least 93%, such as at least 94%, such as at least 95%, such as at least
96%, such as at least 97%, such as at least 98%, such as at least 99% identity thereto.

- 5 These desaturases have been found to preferentially catalyse desaturation of C14
substrates when expressed in a yeast cell.

In such cells, the ratio of desaturated tetradecanoyl-CoA to desaturated hexadecanoyl-
CoA is of at least 0.1, such as at least 0.2, such as at least 0.3, such as at least 0.4,
10 such as at least 0.5, such as at least 0.75, such as at least 1, such as at least 2, such
as at least 3, such as at least 4, such as at least 5, such as at least 6, such as at least
7, such as at least 8, such as at least 9, such as at least 10, such as at least 12.5, such
as at least 15, or more.

15 In some embodiments, the titre of desaturated fatty alcohols is of at least 1 mg/L, such
as at least 1.5 mg/L, such as at least 5 mg/L, such as at least 10 mg/L, such as at least
25 mg/L, such as at least 50 mg/L, such as at least 100 mg/L, such as at least 250
mg/L, such as at least 500 mg/L, such as at least 750 mg/L, such as at least 1 g/L,
such as at least 2 g/L, such as at least 3 g/L, such as at least 4 g/L, such as at least 5
20 g/L, or more.

In some embodiments, the titre of desaturated fatty alcohol having a chain length of 14
is of at least 1 mg/L, such as at least 1.5 mg/L, such as at least 5 mg/L, such as at
least 10 mg/L, such as at least 25 mg/L, such as at least 50 mg/L, such as at least 100
25 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at least 750 mg/L,
such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L, such as at least 4
g/L, such as at least 5 g/L, or more.

In some embodiments, desaturated fatty alcohols are yielded comprising at least 1% of
30 a desaturated fatty alcohol having a chain length of 14, such as at least 1.5%, such as
at least 2%, such as at least 2.5%, such as at least 3%, such as at least 3.5%, such as
at least 4%, such as at least 4.5%, such as at least 5%, such as at least 7.5%, such as
at least 10%, or more.

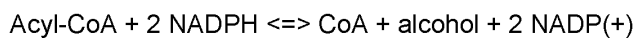
How to test whether a given desaturase has the required specificity can be done as described herein.

Fatty acyl-CoA reductase

- 5 The terms 'fatty acyl-CoA reductase' and 'FAR' will be used herein interchangeably. The term 'heterologous FAR' refers to a FAR which is not naturally expressed by the organism, such as by the cell.

FARs catalyze the two-step reaction:

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wherein in a first step, the fatty acyl-CoA is reduced to a fatty aldehyde, before the fatty aldehyde is further reduced into a fatty alcohol in a second step. The fatty acyl-CoA
15 may be a desaturated or a saturated fatty acyl-CoA.

The FARs capable of catalyzing such reaction are alcohol-forming fatty acyl-CoA reductases with an EC number 1.2.1.84.

- 20 Ncb5ors can increase the activity of FARs. In some embodiments, the first enzyme or group of enzymes comprises or consists of one or more FARs.

- The FAR may be heterologous to the cell disclosed herein. In some embodiments, the FAR is preferably native to an insect such as an insect of the *Lepidoptera* order, such
25 as of the genus *Lepidoptera* order, such as of the genus *Agrotis*, *Amyelois*, *Bicyclus*, *Bombus*, *Chilo*, *Chrysodeixis*, *Cydia*, *Helicoverpa*, *Heliothis*, *Manducta*, *Ostrinia*, *Plodia*, *Plutella*, *Spodoptera*, *Trichoplusia* Tyta or *Yponomeuta*, such as *Agrotis segetum*, *Amyelois transitella*, *Bicyclus anynana*, *Bombus lapidaries*, *Chilo suppressalis*, *Chrysodeixis includes*, *Cydia pomonella*, *Helicoverpa armigera*,
30 *Helicoverpa assulta*, *Heliothis virescens*, *Heliothis subflexa*, *Manducta sexta*, *Ostrinia furnacalis*, *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*, *Spodoptera frugiperda*, *Spodoptera littoralis*, *Spodoptera litura*, *Trichoplusia ni*, *Tyta alba*, *Yponomeuta rorellus*, or a functional variant having at least 60% identity thereto. In some embodiments, the FAR is native to a bacteria, such as of the genus
35 *Marinobacter*, such as *Marinobacter algicola*.

In one embodiment, the heterologous FAR is an *Agrotis* FAR. In one embodiment, the FAR is an *Agrotis segetum* FAR, such as the FAR as set forth in SEQ ID NO: 77 (FAR12). In some embodiments, the FAR is an *Agrotis ipsilon* FAR, such as the FAR as set forth in SEQ ID NO: 78 (FAR18). In some embodiments, the FAR is a variant of an *Agrotis* FAR, a variant of an *Agrotis segetum* FAR, such as the FAR as set forth in SEQ ID NO: 77 (FAR12), a variant of an *Agrotis ipsilon* FAR, such as the FAR as set forth in SEQ ID NO: 78 (FAR18) or a variant thereof, having at least 60% identity thereto.

In one embodiment, the heterologous FAR is an *Amyelois* FAR. In one embodiment, the FAR is an *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 154 (FAR33), SEQ ID NO: 155 (FAR34) or SEQ ID NO: 156 (FAR35). In some embodiments, the FAR is a variant of an *Amyelois* FAR, a variant of an *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 77 (FAR12), a variant of an *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 154 (FAR33), SEQ ID NO: 155 (FAR34) or SEQ ID NO: 156 (FAR35) or a variant thereof, having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Bicyclus* FAR. In one embodiment, the FAR is a *Bicyclus anynana* FAR, such as the FAR as set forth in SEQ ID NO: 79 (FAR11). In some embodiments, the FAR is a variant of a *Bicyclus* FAR, a variant of a *Bicyclus anynana* FAR or a variant of the FAR set forth in SEQ ID NO: 79 (FAR11), having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Bombus* FAR. In one embodiment, the FAR is a *Bombus lapidarius* FAR, such as the FAR as set forth in SEQ ID NO: 80 (FAR14). In some embodiments, the FAR is a variant of a *Bombus* FAR, a variant of a *Bombus lapidarius* FAR or a variant of the FAR set forth in SEQ ID NO: 80 (FAR14), having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Chilo* FAR. In one embodiment, the FAR is a *Chilo suppressalis* FAR, such as the FAR as set forth in SEQ ID NO: 81 (FAR13). In some embodiments, the FAR is a variant of a *Chilo* FAR, a variant of a

Chilo suppressalis FAR or a variant of the FAR set forth in SEQ ID NO: 81 (FAR13), having at least 60% identity thereto.

5 In one embodiment, the heterologous FAR is a *Chrysodeixis* FAR. In one embodiment, the FAR is a *Chrysodeixis includens* FAR, such as the FAR as set forth in SEQ ID NO: 157 (FAR47). In some embodiments, the FAR is a variant of a *Chrysodeixis* FAR, a variant of a *Chrysodeixis includens* FAR or a variant of the FAR set forth in SEQ ID NO: 157 (FAR47), having at least 60% identity thereto.

10 In one embodiment, the heterologous FAR is a *Cydia* FAR. In one embodiment, the FAR is a *Cydia pomonella* FAR, such as the FAR as set forth in SEQ ID NO: 82 (FAR23). In some embodiments, the FAR is a variant of a *Cydia* FAR, a variant of a *Cydia pomonella* FAR or a variant of the FAR set forth in SEQ ID NO: 82 (FAR23), having at least 60% identity thereto.

15 In one embodiment, the heterologous FAR is a *Helicoverpa* FAR. In one embodiment, the FAR is a *Helicoverpa armigera* FAR. In one embodiment, the FAR is a *Helicoverpa armigera* FAR, such as the FAR as set forth in SEQ ID NO: 83 (FAR1). In one embodiment, the FAR is a *Helicoverpa assulta* FAR, such as the FAR as set forth in
20 SEQ ID NO: 84 (FAR6). In some embodiments, the FAR is a variant of a *Helicoverpa* FAR, a variant of a *Helicoverpa armigera* FAR, a variant of a *Helicoverpa armigera* FAR, a variant of a *Helicoverpa assulta* FAR such as a variant of the FAR set forth in SEQ ID NO: 83 (FAR1) or of the FAR set forth in SEQ ID NO: 84 (FAR6), having at least 60% identity thereto.

25 In one embodiment, the heterologous FAR is a *Heliothis* FAR. In one embodiment, the FAR is a *Heliothis subflexa* FAR, such as the FAR as set forth in SEQ ID NO: 85 (FAR4). In one embodiment, the FAR is a *Heliothis virescens* FAR, such as the FAR as set forth in SEQ ID NO: 86 (FAR5). In some embodiments, the FAR is a variant of a
30 *Heliothis* FAR, a variant of a *Heliothis subflexa* FAR, a variant of a *Heliothis virescens* FAR, a variant of the FAR set forth in SEQ ID NO: 85 (FAR4), or of the FAR as set forth in SEQ ID NO: 86 (FAR5), having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Manducta* FAR. In one embodiment,
35 the FAR is a *Manducta sexta* FAR, such as the FAR as set forth in SEQ ID NO: 160

(FAR43). In some embodiments, the FAR is a variant of a *Manducta* FAR, a variant of a *Manducta sexta* FAR or a variant of the FAR set forth in SEQ ID NO: 160 (FAR43), having at least 60% identity thereto.

5 In one embodiment, the heterologous FAR is a *Marinobacter* FAR. In one embodiment, the FAR is a *Marinobacter algicola* FAR, such as the FAR as set forth in SEQ ID NO: 159 (FAR42). In some embodiments, the FAR is a variant of a *Marinobacter* FAR, a variant of a *Marinobacter algicola* FAR or a variant of the FAR set forth in SEQ ID NO: 159 (FAR42), having at least 60% identity thereto.

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In one embodiment, the heterologous FAR is an *Ostrinia* FAR. In one embodiment, the FAR is an *Ostrinia furnacalis* FAR, such as the FAR as set forth in SEQ ID NO: 161 (FAR44). In some embodiments, the FAR is a variant of an *Ostrinia* FAR, a variant of an *Ostrinia furnacalis* FAR or a variant of the FAR set forth in SEQ ID NO: 161 (FAR44), having at least 60% identity thereto.

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In one embodiment, the heterologous FAR is a *Plodia* FAR. In one embodiment, the FAR is a *Plodia interpunctella* FAR, such as the FAR as set forth in SEQ ID NO: 162 (FAR28) or in SEQ ID NO: 163 (FAR30). In some embodiments, the FAR is a variant of a *Plodia* FAR, a variant of a *Plodia interpunctella* FAR or a variant of the FAR set forth in SEQ ID NO: 162 (FAR28) or in SEQ ID NO: 163 (FAR30), having at least 60% identity thereto.

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In one embodiment, the heterologous FAR is a *Plutella* FAR. In one embodiment, the FAR is a *Plutella xylostella* FAR, such as the FAR as set forth in SEQ ID NO: 87 (FAR27). In some embodiments, the FAR is a variant of a *Plutella* FAR, a variant of a *Plutella xylostella* FAR or a variant of the FAR set forth in SEQ ID NO: 87 (FAR27), having at least 60% identity thereto.

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30 In one embodiment, the heterologous FAR is a *Spodoptera* FAR. In one embodiment, the FAR is a *Spodoptera exigua* FAR, such as the FAR as set forth in SEQ ID NO: 88 (FAR16). In one embodiment, the FAR is a *Spodoptera frugiperda* FAR, such as the FAR as set forth in SEQ ID NO: 89 (FAR22). In one embodiment, the FAR is a *Spodoptera littoralis* FAR, such as the FAR as set forth in SEQ ID NO: 90 (FAR15). In one embodiment, the FAR is a *Spodoptera litura* FAR, such as the FAR as set forth in

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SEQ ID NO: 91 (FAR19). In some embodiments, the FAR is a variant of a *Spodoptera* FAR, a variant of a *Spodoptera exigua* FAR, a variant of a *Spodoptera frugiperda* FAR, a variant of a *Spodoptera littoralis* FAR, a variant of a *Spodoptera littura* FAR, a variant of the FAR set forth in SEQ ID NO: 88 (FAR16), a variant of the FAR set forth in SEQ ID NO: 89 (FAR22), a variant of the FAR set forth in SEQ ID NO: 90 (FAR15), a variant of the FAR set forth in SEQ ID NO: 91 (FAR19), having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Tyta* FAR. In one embodiment, the FAR is a *Tyta alba* FAR, such as FAR25 as set forth in SEQ ID NO: 92. In some embodiments, the FAR is a variant of a *Tyta* FAR, a variant of a *Tyta alba* FAR or a variant of FAR25 as set forth in SEQ ID NO: 92, having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Trichoplusia* FAR. In one embodiment, the FAR is a *Trichoplusia ni* FAR, such as FAR38 as set forth in SEQ ID NO: 93. In some embodiments, the FAR is a variant of a *Trichoplusia* FAR, a variant of a *Trichoplusia ni* FAR or a variant of FAR38 as set forth in SEQ ID NO: 93, having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Trichoplusia* FAR. In one embodiment, the FAR is a *Trichoplusia ni* FAR, such as FAR41 as set forth in SEQ ID NO: 166. In some embodiments, the FAR is a variant of a *Trichoplusia* FAR, a variant of a *Trichoplusia ni* FAR or a variant of FAR41 as set forth in SEQ ID NO: 166, having at least 60% identity thereto.

In one embodiment, the heterologous FAR is a *Yponomeuta* FAR. In one embodiment, the FAR is a *Yponomeuta rorellus* FAR, such as FAR8 as set forth in SEQ ID NO: 167. In some embodiments, the FAR is a variant of a *Yponomeuta* FAR, a variant of a *Yponomeuta rorellus* FAR or a variant of FAR8 as set forth in SEQ ID NO: 167, having at least 60% identity thereto.

It will be understood that a variant FAR having at least 60% identity to a given FAR as above may have at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such

as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%,
such as at least 76%, such as at least 77%, such as at least 78%, such as at least
79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at
least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as
5 at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such
as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%,
such as at least 95%, such as at least 96%, such as at least 97%, such as at least
98%, such as at least 99% identity to the FAR, or more.

10 Nucleic acids encoding FARs

In some embodiments, the heterologous FAR is encoded by a nucleic acid having at
least 60% identity to a nucleic acid selected from the group of desaturases set forth in
SEQ ID NOs: 94 to 110 and SEQ ID NOs: 168-181, such as at least 61% identity, such
as at least 62% identity, such as at least 63% identity, such as at least 64% identity,
15 such as at least 65% identity, such as at least 66% identity, such as at least 67%
identity, such as at least 68% identity, such as at least 69% identity, such as at least
70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%,
such as at least 74%, such as at least 75%, such as at least 76%, such as at least
77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at
20 least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as
at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such
as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%,
such as at least 93%, such as at least 94%, such as at least 95%, such as at least
96%, such as at least 97%, such as at least 98%, such as at least 99% identity, such
25 as 100% identity thereto.

In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least
60% identity to the nucleic acid encoding a FAR from *Agrotis segetum*, as set forth in
SEQ ID NO: 94. In one embodiment, the heterologous FAR is encoded by a nucleic
30 acid having at least 60% identity to the nucleic acid encoding a FAR from *Agrotis*
ipsilon, as set forth in SEQ ID NO: 95. In one embodiment, the heterologous FAR is
encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a
FAR from *Amyelois transitella*, as set forth in SEQ ID NO: 168, SEQ ID NO: 169 or
SEQ ID NO: 170. In one embodiment, the heterologous FAR is encoded by a nucleic
35 acid having at least 60% identity to the nucleic acid encoding a FAR from *Bicyclus*

anyana, as set forth in SEQ ID NO: 96. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Bombus lapidarius*, as set forth in SEQ ID NO: 97. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Chilo suppressalis*, as set forth in SEQ ID NO: 98. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Chrysodeixis includens*, as set forth in SEQ ID NO: 171. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Cydia pomonella*, as set forth in SEQ ID NO: 99 or SEQ ID NO: 172. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Helicoverpa armigera*, as set forth in SEQ ID NO: 100. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Helicoverpa assulta*, as set forth in SEQ ID NO: 101. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Heliothis subflexa*, as set forth in SEQ ID NO: 102. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Heliothis virescens*, as set forth in SEQ ID NO: 103. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Marinobacter algicola*, as set forth in SEQ ID NO: 173. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Manducta sexta*, as set forth in SEQ ID NO: 174. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Ostrinia furnacalis*, as set forth in SEQ ID NO: 175. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Plodia interpunctella*, as set forth in SEQ ID NO: 176 or SEQ ID NO: 177. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Plutella xylostella*, as set forth in SEQ ID NO: 104. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Spodoptera exigua*, as set forth in SEQ ID NO: 105, SEQ ID NO: 178 or SEQ ID NO: 179. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a

FAR from *Spodoptera frugiperda*, as set forth in SEQ ID NO: 106. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Spodoptera littoralis*, as set forth in SEQ ID NO: 107. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Spodoptera litura*, as set forth in SEQ ID NO: 108. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Tyta alba*, as set forth in SEQ ID NO: 109. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Trichoplusia ni*, as set forth in SEQ ID NO: 110 or SEQ ID NO: 180. In one embodiment, the heterologous FAR is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding a FAR from *Yponomeuta rorellus*, as set forth in SEQ ID NO: 181. Herein, a nucleic acid having at least 60% identity to a given nucleic acid may have at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% to the given nucleic acid, or more.

Co-expression of a plurality of FARs

The present cells may express at least one heterologous FAR. In some embodiments, the cell expresses one heterologous FAR. It may however be desirable to express several heterologous FARs, such as at least two heterologous FARs, which may be identical or different. Alternatively, it may be desirable to express several copies of the nucleic acid encoding the at least one heterologous FAR, such as at least two copies, at least three copies or more. In other embodiments, the cell expresses at least two heterologous FARs, for example three heterologous FARs.

For example, the cell may express two copies of FAR1 or a variant thereof; or one copy of FAR1 and one copy of FAR5; or two copies of FAR1, one copy of FAR5 and one copy of FAR4.

5 Desaturases and FARs

Any of the above FARs can be expressed together with any desaturase, in particular any of the desaturases described herein.

In some embodiments, the cell expresses:

- 10 - an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16
- 15 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase,
- 20 such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11;
- 25 a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis*
- 30 desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a
- 35 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO:

- 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and
- an Ncb5or as detailed below,
- or variants thereof having at least 60% identity thereto.
- In other embodiments, the cell expresses:
- an *Agrotis* FAR, such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78, and/or
 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16

as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as

set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a

5 *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set

10 forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and

- an Ncb5or as detailed below,

or variants thereof having at least 60% identity thereto.

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In other embodiments, the cell expresses:

- a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ
- 20 ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a
- 25 *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in
- 30 SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example
- 35

Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and

- an Ncb5or as detailed below,

or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80, and/or
- 5 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a
- 10 *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for
- 15 example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a
- 20 *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or
- 25 Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example
- 30 Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set
- 35 forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium*

- 5 *hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a
Plutella desaturase, such as a *Plutella xylostella* desaturase, for example
 Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a
Ricinus communis desaturase, for example Desat23 as set forth in SEQ ID NO:
 10 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae*
 desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera*
 desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as
 set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for
 example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ
 15 ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as
 set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a
Thaumetopoea desaturase, such as a *Thaumetopoea pityocampa* desaturase,
 for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase,
 such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in
 20 SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia*
 desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set
 forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica*
 desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or
 combinations thereof; and
 - an Ncb5or as detailed below,
 or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- 25 - a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth
 in SEQ ID NO: 81, and/or
 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum*
 desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois*
 desaturase, such as an *Amyelois transitella* desaturase, for example Desat16
 30 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18
 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a
Chauliognathus lugubris desaturase, for example Desat25 as set forth in SEQ
 ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for
 example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase,
 such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth
 35 in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for

example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in

- SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or
- 5 combinations thereof; and
- an Ncb5or as detailed below,
- or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- 10 - a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16
- 15 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase,
- 20 such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11;
- 25 a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis*
- 30 desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a
- 35 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO:

19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and

- an Ncb5or as detailed below,

or variants thereof having at least 60% identity thereto.

30 In other embodiments, the cell expresses:

- a *Helicoverpa* FAR, such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 83 or a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 82; and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois*

desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera*

- desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a
- 5 *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia*
- 10 desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and
- an Ncb5or as detailed below,
- 15 or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- a *Heliothis* FAR, such as a *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85 or a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86; and/or
- 20 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18
- 25 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth
- 30 in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for
- 35 example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such

as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and

- an Ncb5or as detailed below,
or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- 5 - a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth in SEQ ID NO: 87, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16
- 10 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase,
- 15 such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11;
- 20 a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis*
- 25 desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a
- 30 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manduca* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for
- 35 example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase,

- such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and
- an Ncb5or as detailed below,
- or variants thereof having at least 60% identity thereto.
- In other embodiments, the cell expresses:
- a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, a *Spodoptera frugiperda* FAR, for example FAR22 as set forth in SEQ ID NO: 89, a *Spodoptera littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91, and/or
 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a

Chauliognathus lugubris desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manduca* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ

- ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and
- an Ncb5or as detailed below,
- or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses:

- a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas*

desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33
 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita*
molesta desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or
 Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a
 5 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO:
 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example
 Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO:
 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO:
 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for
 10 example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase,
 such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set
 forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium*
hortorum desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a
 15 *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example
 Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a
Ricinus communis desaturase, for example Desat23 as set forth in SEQ ID NO:
 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae*
 desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera*
 20 desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as
 set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for
 example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ
 ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as
 set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a
 25 *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase,
 for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase,
 such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in
 SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia*
 desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set
 forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica*
 30 desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or
 combinations thereof; and
 - an Ncb5or as detailed below,
 or variants thereof having at least 60% identity thereto.

35 In other embodiments, the cell expresses:

- a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93, and/or
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example

Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and

- an Ncb5or as detailed below,

or variants thereof having at least 60% identity thereto.

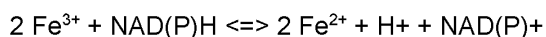
The term "variant thereof having at least 60% identity" in relation to a given enzyme shall be understood to refer to variants having 60% identity or more to said enzyme, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to the enzyme, or more.

NAD(P)H cytochrome b5 oxidoreductase

While expression of one or more heterologous desaturases and/or one or more reductases can result in the production of desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, and/or saturated fatty alcohol acetates, the
5 inventors have found that introduction of an additional enzyme in the cell appears to have a positive effect on the activity of the desaturase and/or reductase, as it results in an increase in titer. This additional enzyme is an NAD(P)H cytochrome b5 oxidoreductase, and is naturally found in a number of insects, including of the Lepidoptera order.

10 The term 'NAD(P)H cytochrome b5 oxidoreductase' and 'Ncb5or' will be used herein interchangeably. The term 'heterologous Ncb5or' refers to an Ncb5or which is not naturally expressed by the organism, such as by the cell.

15 Ncb5or is also known as cytochrome b5 reductase 4 and is an oxidoreductase acting on NADH or NADPH, with a heme protein as acceptor. It contains three functional domains similar to cytochrome b5, cytochrome b5 reductase and CHORD-SGT1 (Deng, et al., 2010). Ncb5ors catalyze the reaction:



Ncb5ors capable of catalyzing such reaction have EC number 1.6.2.2.

25 The cell disclosed herein expresses a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or); whereby the cell is capable of producing the compound with a higher titer compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when
30 cultivated in the same conditions.

In one embodiment, the first enzyme or group of enzymes may consist of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA, whereby the cell is capable of producing a desaturated fatty acyl-CoA with a higher titer

compared to a cell expressing said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.

5 In another embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) capable of converting a fatty acyl-CoA to a saturated fatty alcohol, whereby the cell is capable of producing a saturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR but no heterologous Ncb5or when cultivated in the same conditions.

10 In yet another embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol, whereby the cell is capable of producing a desaturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR and said one or more desaturase but no heterologous Ncb5or when
15 cultivated in the same conditions.

The cell may further express an acetyltransferase, whereby said cell is capable of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively, whereby the cell is capable of producing a
20 desaturated or a saturated fatty alcohol acetate with a higher titer compared to a cell expressing the first group of enzymes and the acetyltransferase but no heterologous Ncb5or when cultivated in the same conditions.

In a preferred embodiment, the production of said desaturated fatty alcohol, saturated
25 fatty alcohol, desaturated fatty alcohol acetate, saturated fatty alcohol acetate, and a desaturated fatty acyl-CoA is increased in said organism compared to the production of said desaturated fatty alcohol, saturated fatty alcohol, desaturated fatty alcohol acetate, saturated fatty alcohol acetate, and a desaturated fatty acyl-CoA in an organism cultivated in the same conditions and not expressing said heterologous Ncb5or. In
30 other words, expression of a heterologous Ncb5or increases the production of said desaturated fatty alcohol, saturated fatty alcohol, desaturated fatty alcohol acetate, saturated fatty alcohol acetate, and a desaturated fatty acyl-CoA in a cell expressing said first enzyme or group of enzymes. Thus, expression of a heterologous Ncb5or increases the activity of said said first enzyme or group of enzymes, such as said
35 heterologous desaturase and/or of said heterologous FAR compared to the activity of

said heterologous desaturase and/or said heterologous FAR in the absence of said heterologous Ncb5or, when tested in identical or similar conditions, wherein the activity is measured e.g. by measuring the titer of product formed by the heterologous desaturase and the heterologous FAR.

5

Further provided herein is the use of an Ncb5or in a method for increasing the activity of one or more enzymes.

10 In one embodiment, the one or more enzymes is one or more membrane-bound enzymes. The skilled person knows how to determine whether an enzyme is membrane-bound. For instance, fluorescent markers can be used, to determine whether an enzyme fused to a fluorescent marker colocalises with a protein which is known to be found in the membrane.

15 In one embodiment, the one or more enzymes is selected from the group consisting of desaturases and fatty acyl reductases, such as the desaturases and fatty acyl reductases presented herein in the sections "Desaturase" and "Fatty acyl-CoA reductase", respectively.

20 In one embodiment, the increase in activity of said of one or more enzymes, for example a desaturase and/or a FAR as described herein, is at least 1.2-fold, such as at least 1.3-fold, such as at least 1.4-fold, such as at least 1.5-fold, such as at least 1.6-fold, such as at least 1.7-fold, such as at least 1.8-fold, such as at least 1.9-fold, such as at least 2-fold, such as at least 3-fold, such as at least 4-fold, such as at least 5-fold,
25 such as at least 6-fold, such as at least 7-fold, such as at least 8-fold, such as at least 9-fold, such as at least 10-fold, such as at least 15-fold, such as at least 20-fold, such as at least 30-fold, such as at least 40-fold, such as at least 50-fold; wherein the increase in activity of said of one or more enzymes is compared to the activity of said one or more enzymes in the absence of said Ncb5or, wherein the activity is measured
30 under the same conditions, wherein the increase is measured by measuring the concentration of product formed by the one or more enzymes.

In one embodiment, the increase in activity of said of one or more enzymes, for example a desaturase and/or a FAR as described herein, is at least 1.2-fold, such as at
35 least 1.3-fold, such as at least 1.4-fold, such as at least 1.5-fold, such as at least 1.6-

fold, such as at least 1.7-fold, such as at least 1.8-fold, such as at least 1.9-fold, such as at least 2-fold, such as at least 3-fold, such as at least 4-fold, such as at least 5-fold, such as at least 6-fold, such as at least 7-fold, such as at least 8-fold, such as at least 9-fold, such as at least 10-fold, such as at least 15-fold, such as at least 20-fold, such as at least 30-fold, such as at least 40-fold, such as at least 50-fold; wherein the increase in activity of said one or more enzymes is compared to the activity of said one or more enzymes in the absence of said Ncb5or, wherein the activity is measured under the same conditions, wherein the increase is measured by measuring the concentration of product formed by the desaturase and/or the FAR.

The Ncb5ors disclosed herein may be any type of Ncb5or. In some embodiments, the Ncb5or is native to a plant, an insect or a mammal. In some embodiments, the Ncb5or is native to an insect, such as an insect of the genus *Agrotis*, *Amyelois*, *Aphantopus*, *Arctia*, *Bicyclus*, *Bombus*, *Bombyx*, *Chilo*, *Cydia*, *Danaus*, *Drosophila*, *Eumeta*, *Galleria*, *Helicoverpa*, *Heliothis*, *Hypocmocoma*, *Leptidea*, *Lobesia*, *Manduca*, *Operophtera*, *Ostrinia*, *Papilio*, *Papilio*, *Papilio*, *Pieris*, *Plutella*, *Spodoptera*, *Trichoplusia*, and *Vanessa*. In preferred embodiments, the Ncb5or is native to an insect selected from *Agrotis segetum*, *Amyelois transitella*, *Aphantopus hyperantus*, *Arctia plantaginis*, *Bicyclus anynana*, *Bombus terrestris*, *Bombyx mandarina*, *Bombyx mori*, *Chilo suppressalis*, *Cydia pomonella*, *Danaus plexippus*, *Drosophila grimshawi*, *Drosophila melanogaster*, *Eumeta japonica*, *Galleria mellonella*, *Helicoverpa armigera*, *Heliothis virescens*, *Hypocmocoma kahanamoo*, *Leptidea sinapis*, *Lobesia botrana*, *Manduca sexta*, *Operophtera brumata*, *Ostrinia furnacalis*, *Papilio machaon*, *Papilio polytes*, *Papilio xuthus*, *Pieris rapae*, *Plutella xylostella*, *Spodoptera frugiperda*, *Spodoptera litura*, *Trichoplusia ni*, and *Vanessa tameamea*.

In some embodiments, the Ncb5or is an Ncb5or selected from Table 5.

In some embodiments, the Ncb5or is an Ncb5or selected from the group of Ncb5ors as set forth in SEQ ID NOs: 111 to 114, SEQ ID NO: 124 or SEQ ID NOs: 182 to 185, or variants thereof having at least 60% identity to an Ncb5or selected from the group of Ncb5ors set forth in SEQ ID NOs: 111 to 114, SEQ ID NO: 124 or SEQ ID NOs: 182 to 185.

In one embodiment, the Ncb5or is a *Cydia* Ncb5or. In one embodiment, the Ncb5or is a *Cydia pomonella* Ncb5or. In some embodiments, the Ncb5or is a variant of a *Cydia* Ncb5or as set forth in SEQ ID NO: 124 (CpoNcb5or1) or SEQ ID NO: 182 (CpNcb5or), or a variant thereof having at least 60% identity thereto.

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In one embodiment, the Ncb5or is a *Drosophila* Ncb5or. In one embodiment, the Ncb5or is a *Drosophila melanogaster* Ncb5or. In one embodiment, the Ncb5or is a *Drosophila virilis* Ncb5or. In some embodiments, the Ncb5or is a variant of a *Drosophila* Ncb5or, a variant of a *Drosophila melanogaster* Ncb5or, a variant of a *Drosophila grimshawi* Ncb5or, a variant of the Ncb5or as set forth in SEQ ID NO: 112 (DmNcb5or), or a variant of the Ncb5or as set forth in SEQ ID NO: 111 (DgNcb5or), having at least 60% identity to the Ncb5or set forth in SEQ ID NO: 112 or SEQ ID NO: 111.

10

15

In one embodiment, the Ncb5or is a *Homo* Ncb5or. In one embodiment, the Ncb5or is a *Homo sapiens* Ncb5or. In some embodiments, the Ncb5or is a variant of a *Homo* Ncb5or, a variant of a *Homo sapiens* Ncb5or or a variant of the Ncb5or as set forth in SEQ ID NO: 113 (HsNcb5or), having at least 60% identity to the Ncb5or set forth in SEQ ID NO: 113.

20

In one embodiment, the Ncb5or is a *Lobesia* Ncb5or. In one embodiment, the Ncb5or is a *Lobesia botrana* Ncb5or, such as set forth in SEQ ID NO: 189 (LboNcb5or). In some embodiments, the Ncb5or is a variant of a *Lobesia* Ncb5or such as set forth in SEQ ID NO: 189, having at least 60% identity thereto.

25

In some embodiments, the Ncb5or is a *Bombus* Ncb5or. In one embodiment, the Ncb5or is a *Bombus terrestris* Ncb5or, such as set forth in SEQ ID NO: 184 (BterNcb5or), or a variant thereof having at least 60% identity thereto.

30

In one embodiment, the Ncb5or is a *Spodoptera* Ncb5or. In one embodiment, the Ncb5or is a *Spodoptera litura* Ncb5or. In some embodiments, the Ncb5or is a variant of a *Spodoptera* Ncb5or, a variant of a *Spodoptera litura* Ncb5or or a variant of the Ncb5or as set forth in SEQ ID NO: 114 (SlitNcb5or), having at least 60% identity to the Ncb5or set forth in SEQ ID NO: 114.

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A variant of an Ncb5or refers to a functional variant of an Ncb5or, which retains at least some or all of the Ncb5or activity, and which has at least 60% identity, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99%, such as 100% identity thereto.

Nucleic acids encoding Ncb5ors

In some embodiments, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to an Ncb5or selected from the group of Ncb5ors set forth in SEQ ID NOs: 115 to 118. Such nucleic acids may be introduced in a cell as described herein, or may be comprised within a vector such as a plasmid, as is known in the art.

In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to a nucleic acid encoding an *Agrotis segetum* Ncb5or, such as the nucleic acid sequence as set forth in SEQ ID NO: 187. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to a nucleic acid encoding a *Bombus terrestris* Ncb5or, such as the nucleic acid sequence as set forth in SEQ ID NO: 188. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to a nucleic acid encoding a *Cydia pomonella* Ncb5or, such as the nucleic acid sequence as set forth in SEQ ID NO: 125 or SEQ ID NO: 182. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding the Ncb5or from *Drosophila grimshawi* as set forth in SEQ ID NO: 115. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding the Ncb5or from *Drosophila melanogaster* as set forth in SEQ ID NO: 116. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid

having at least 60% identity to the nucleic acid encoding the Ncb5or from *Homo sapiens* as set forth in SEQ ID NO: 117. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to a nucleic acid encoding a *Lobesia botrana* Ncb5or, such as the nucleic acid sequence as set forth in SEQ ID NO: 185. In one embodiment, the heterologous Ncb5or is encoded by a nucleic acid having at least 60% identity to the nucleic acid encoding the Ncb5or from *Spodoptera litura* as set forth in SEQ ID NO: 118.

Herein a nucleic acid having at least 60% identity to a given nucleic acid has at least 60% identity, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99%, such as 100% identity thereto.

Co-expression of a plurality of Ncb5ors

The present cells express at least one heterologous Ncb5or. In some embodiments, the cell expresses one heterologous Ncb5or. It may however be desirable to express several heterologous Ncb5ors, such as at least two heterologous Ncb5ors, which may be identical or different. Alternatively, it may be desirable to express several copies of the nucleic acid encoding the at least one heterologous Ncb5or, such as at least two copies, at least three copies or more. In some embodiments, the cell expresses at least two heterologous Ncb5ors, for example three heterologous Ncb5ors.

Desaturases, FARs and Ncb5ors

Any of the above Ncb5ors can be expressed in the cell together with any combination of desaturase and reductase described herein. The Ncb5ors listed herein below can

thus be used to increase the activity of any of the FARs and/or desaturases listed herein below, not only in vivo, but also in vitro.

In some embodiments, the cell expresses a *Cydia* Ncb5or, such as a *Cydia pomonella* Ncb5or, for example CpoNcb5or1 (SEQ ID NO: 124) or CpNcb5or (SEQ ID NO: 182); and one or both of:

- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manduca* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase,

such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or

- a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a *Helicoverpa* FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85; a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth

in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda* FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a
5 *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91; a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93;

or variants thereof having at least 60% identity thereto.

10 In other embodiments, the cell expresses a *Drosophila* Ncb5or, such as a *Drosophila grimshawi* Ncb5or, for example DgNcb5or as set forth in SEQ ID NO: 111; and one or both of:

- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum*
15 desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ
20 ID NO: 5; a *Chilo* desaturase, such as a *Chilo supprealis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a
25 *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in
30 SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or
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- Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or
- a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia*

5 *pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a
Helicoverpa FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as
 set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example
 FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis*
 10 *virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a
Heliothis subflexa FAR, for example FAR4 as set forth in SEQ ID NO: 85; a
Plutella FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth
 in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for
 example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda*
 15 FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera*
littoralis FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a
Spodoptera litura FAR, for example FAR19 as set forth in SEQ ID NO: 91; a
Tyta FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID
 NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example
 20 FAR38 as set forth in SEQ ID NO: 93;
 or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses a *Drosophila* Ncb5or, such as a *Drosophila*
melanogaster Ncb5or, for example DmNcb5or as set forth in SEQ ID NO: 112; and one
 25 or both of:

- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum*
 desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois*
 desaturase, such as an *Amyelois transitella* desaturase, for example Desat16
 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18
 30 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a
Chauliognathus lugubris desaturase, for example Desat25 as set forth in SEQ
 ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for
 example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase,
 such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth
 35 in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for
 example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a
Cydia pomonella desaturase, for example Desat4 as set forth in SEQ ID NO: 9,
 Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11;
 a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for
 example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such

as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or

- a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a *Helicoverpa* FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85; a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda* FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91; a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93;

or variants thereof having at least 60% identity thereto.

- 25 In other embodiments, the cell expresses a *Homo* Ncb5or, such as a *Homo sapiens* Ncb5or, for example HsNcb5or as set forth in SEQ ID NO: 113; and one or both of:
- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth

in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11;

5 a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis*

10 desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a

15 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for

20 example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example

25 Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as

30 set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase,

35 for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase,

such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or

- a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a *Helicoverpa* FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85; a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda* FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91; a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93;

or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses a *Lobesia* Ncb5or, such as a *Lobesia botrana* Ncb5or; and one or both of:

- a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16

as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as

- set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a
- 5 *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set
- 10 forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or
- a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon*
 - 15 FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a
 - 20 *Helicoverpa* FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a
 - 25 *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85; a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda* FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera*
 - 30 *littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91; a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93;
 - 35 or variants thereof having at least 60% identity thereto.

In other embodiments, the cell expresses a *Spodoptera* Ncb5or, such as a *Spodoptera litura* Ncb5or, for example SlitNcb5or as set forth in SEQ ID NO: 114; and one or both of:

- 5 - a desaturase selected from: an *Agrotis* desaturase, such as an *Agrotis segetum* desaturase, for example Desat19 as set forth in SEQ ID NO: 1; an *Amyelois* desaturase, such as an *Amyelois transitella* desaturase, for example Desat16 as set forth in SEQ ID NO: 2, Desat17 as set forth in SEQ ID NO: 3, or Desat18 as set forth in SEQ ID NO: 4; a *Chauliognathus* desaturase, such as a
10 *Chauliognathus lugubris* desaturase, for example Desat25 as set forth in SEQ ID NO: 5; a *Chilo* desaturase, such as a *Chilo suppressalis* desaturase, for example Desat47 as set forth in SEQ ID NO: 6; a *Choristoneura* desaturase, such as a *Choristoneura parallela* desaturase, for example Desat36 as set forth in SEQ ID NO: 7, or such as a *Choristoneura rosaceana* desaturase, for
15 example Desat35 as set forth in SEQ ID NO: 8; a *Cydia* desaturase, such as a *Cydia pomonella* desaturase, for example Desat4 as set forth in SEQ ID NO: 9, Desat2 as set forth in SEQ ID NO: 10, or Desat1 as set forth in SEQ ID NO: 11; a *Dendrolimus* desaturase, such as a *Dendrolimus punctatus* desaturase, for example Desat40 as set forth in SEQ ID NO: 12; a *Drosophila* desaturase, such as a
20 *Drosophila grimshawi* desaturase, for example Desat59 as set forth in SEQ ID NO: 13, or such as a *Drosophila melanogaster* desaturase, for example Desat24 as set forth in SEQ ID NO: 14, or such as a *Drosophila virilis* desaturase, for example Desat61 as set forth in SEQ ID NO: 15; or an *Epiphyas* desaturase, such as an *Epiphyas postvittana* desaturase, for example Desat33 as set forth in SEQ ID NO: 16; a *Grapholita* desaturase, such as a *Grapholita molesta* desaturase, for example Desat31 as set forth in SEQ ID NO: 17, or Desat55 as set forth in SEQ ID NO: 18; a *Helicoverpa* desaturase, such as a
25 *Helicoverpa zea* desaturase, for example Desat51 as set forth in SEQ ID NO: 19; a *Lobesia* desaturase, such as a *Lobesia botrana* desaturase, for example Desat30 as set forth in SEQ ID NO: 20 or Desat43 as set forth in SEQ ID NO: 21; a *Manducta* desaturase, for example Desat52 as set forth in SEQ ID NO: 22; an *Ostrinia* desaturase, such as an *Ostrinia nubilalis* desaturase, for example Desat32 as set forth in SEQ ID NO: 23; an *Pectinophora* desaturase, such as an *Pectinophora gossypiella* desaturase, for example Desat48 as set
30 forth in SEQ ID NO: 24; a *Pelargonium* desaturase, such as a *Pelargonium*

- 5 *hortorum* desaturase, for example Desat22 as set forth in SEQ ID NO: 25; a *Plutella* desaturase, such as a *Plutella xylostella* desaturase, for example Desat45 as set forth in SEQ ID NO: 26; a *Ricinus* desaturase, such as a *Ricinus communis* desaturase, for example Desat23 as set forth in SEQ ID NO: 27; a *Saccharomyces* desaturase, such as a *Saccharomyces cerevisiae* desaturase, for example Desat42 as set forth in SEQ ID NO: 28; a *Spodoptera* desaturase, such as a *Spodoptera exigua* desaturase, for example Desat37 as set forth in SEQ ID NO: 29, or such as a *Spodoptera littoralis* desaturase, for example Desat20 as set forth in SEQ ID NO: 30 or Desat20 as set forth in SEQ ID NO: 31, or such as a *Spodoptera litura* desaturase, for example Desat38 as set forth in SEQ ID NO: 32 or Desat26 as set forth in SEQ ID NO: 33; a *Thaumetopoea* desaturase, such as a *Thaumetopoea pityocampa* desaturase, for example Desat34 as set forth in SEQ ID NO: 34; a *Tribolium* desaturase, such as a *Tribolium castaneum* desaturase, for example Desat28 as set forth in SEQ ID NO: 35 or Desat29 as set forth in SEQ ID NO: 36; a *Trichoplusia* desaturase, such as a *Trichoplusia ni* desaturase, for example Desat21 as set forth in SEQ ID NO: 37; a *Yarrowia* desaturase, such as a *Yarrowia lipolytica* desaturase, for example Desat69 as set forth in SEQ ID NO: 38; or combinations thereof; and/or
- 20 - a FAR selected from: an *Agrotis* FAR, such as an *Agrotis segetum* FAR, for example FAR12 as set forth in SEQ ID NO: 77, or such as an *Agrotis ipsilon* FAR, for example FAR18 as set forth in SEQ ID NO: 78; a *Bicyclus* FAR, such as a *Bicyclus anynana* FAR, for example FAR11 as set forth in SEQ ID NO: 79; a *Bombus* FAR, such as a *Bombus lapidarius* FAR, for example FAR14 as set forth in SEQ ID NO: 80; a *Chilo* FAR, such as a *Chilo suppressalis* FAR, for example FAR13 as set forth in SEQ ID NO: 81; a *Cydia* FAR, such as a *Cydia pomonella* FAR, for example FAR23 as set forth in SEQ ID NO: 82; a *Helicoverpa* FAR, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a *Helicoverpa assulta* FAR, for example FAR6 as set forth in SEQ ID NO: 84; a *Heliothis* FAR, such as a *Heliothis virescens* FAR, for example FAR5 as set forth in SEQ ID NO: 86, or such as a *Heliothis subflexa* FAR, for example FAR4 as set forth in SEQ ID NO: 85; a *Plutella* FAR, such as a *Plutella xylostella* FAR, for example FAR27 as set forth in SEQ ID NO: 87; a *Spodoptera* FAR, such as a *Spodoptera exigua* FAR, for example FAR16 as set forth in SEQ ID NO: 88, or a *Spodoptera frugiperda*
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FAR, for example FAR22 as set forth in SEQ ID NO: 89, or a *Spodoptera littoralis* FAR, for example FAR15 as set forth in SEQ ID NO: 90, or a *Spodoptera litura* FAR, for example FAR19 as set forth in SEQ ID NO: 91; a *Tyta* FAR, such as a *Tyta alba* FAR, for example FAR25 as set forth in SEQ ID NO: 92; and a *Trichoplusia* FAR, such as a *Trichoplusia ni* FAR, for example FAR38 as set forth in SEQ ID NO: 93;
or variants thereof having at least 60% identity thereto.

The term "variant having at least 60% identity" in relation to a given enzyme shall be understood to refer to variants having 60% identity or more to said enzyme, such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to the enzyme, or more.

Methods to determine whether an Ncb5or increases the activity of a desaturase and/or a fatty acyl-CoA reductase will be apparent to the person of skill in the art in view of the present disclosure. For example, whether a given Ncb5or increases the activity of a desaturase can be determined by incubating in a solution cells comprising the fatty acyl-CoA substrate for said desaturase, wherein the cells express either (i) said Ncb5or and said desaturase; or (ii) said desaturase. After 48 hours of incubation under the same conditions, the amount (titer) of product (i.e. the amount of desaturated fatty-acyl CoA) generated by the desaturase can be determined by GC-MS. A higher titer from the cells expressing said Ncb5or compared to the cells not expressing said Ncb5or indicates that said Ncb5or increases the activity of said desaturase.

In one embodiment, the Ncb5or is DgNcb5or (SEQ ID NO: 111), the FAR is selected from the group consisting of FAR12 (SEQ ID NO: 77), FAR18 (SEQ ID NO: 78), FAR11 (SEQ ID NO: 79), FAR14 (SEQ ID NO: 80), FAR13 (SEQ ID NO: 81), FAR23 (SEQ ID NO: 82), FAR1 (SEQ ID NO: 83), FAR6 (SEQ ID NO: 84), FAR4 (SEQ ID NO: 85), FAR5 (SEQ ID NO: 86), FAR27 (SEQ ID NO: 87), FAR16 (SEQ ID NO: 88), FAR22 (SEQ ID NO: 89), FAR15 (SEQ ID NO: 90), FAR19 (SEQ ID NO: 91), FAR25 (SEQ ID NO: 92), FAR38 (SEQ ID NO: 93), FAR33 (SEQ ID NO: 154), FAR34 (SEQ ID NO: 155), FAR35 (SEQ ID NO: 156), FAR47 (SEQ ID NO: 157), FAR46 (SEQ ID NO: 158), FAR42 (SEQ ID NO: 159), FAR43 (SEQ ID NO: 160), FAR44 (SEQ ID NO: 161), FAR28 (SEQ ID NO: 162), FAR30 (SEQ ID NO: 163), FAR17 (SEQ ID NO: 164), FAR45 (SEQ ID NO: 165), FAR41 (SEQ ID NO: 166), and FAR8 (SEQ ID NO: 167), and the desaturase is selected from the group consisting of Desat19 (SEQ ID NO: 1), Desat16 (SEQ ID NO: 2), Desat17 (SEQ ID NO: 3), Desat18 (SEQ ID NO: 4), Desat25 (SEQ ID NO: 5), Desat47 (SEQ ID NO: 6), Desat36 (SEQ ID NO: 7), Desat35 (SEQ ID NO: 8), Desat4 (SEQ ID NO: 9), Desat2 (SEQ ID NO: 10), Desat1 (SEQ ID NO: 11), Desat40 (SEQ ID NO: 12), Desat59 (SEQ ID NO: 13), Desat24 (SEQ ID NO: 14), Desat61 (SEQ ID NO: 15), Desat33 (SEQ ID NO: 16), Desat31 (SEQ ID NO: 17), Desat55 (SEQ ID NO: 18), Desat51 (SEQ ID NO: 19), Desat30 (SEQ ID NO: 20), Desat43 (SEQ ID NO: 21), Desat52 (SEQ ID NO: 22), Desat32 (SEQ ID NO: 23), Desat48 (SEQ ID NO: 24), Desat22 (SEQ ID NO: 25), Desat45 (SEQ ID NO: 26), Desat23 (SEQ ID NO: 27), Desat42 (SEQ ID NO: 28), Desat37 (SEQ ID NO: 29), Desat20 (SEQ ID NO: 30), Desat20 (SEQ ID NO: 31), Desat38 (SEQ ID NO: 32), Desat26 (SEQ ID NO: 33), Desat34 (SEQ ID NO: 34), Desat28 (SEQ ID NO: 35), Desat29 (SEQ ID NO: 36), Desat21 (SEQ ID NO: 37), Desat69 (SEQ ID NO: 38), Desat72 (SEQ ID NO: 126), Desat76 (SEQ ID NO: 127), Desat75 (SEQ ID NO: 128), Desat78 (SEQ ID NO: 129), Desat44 (SEQ ID NO: 130), Desat60 (SEQ ID NO: 131), Desat63 (SEQ ID NO: 132), Desat56 (SEQ ID NO: 133), Desat70 (SEQ ID NO: 134), Desat71 (SEQ ID NO: 135), Desat77 (SEQ ID NO: 136), Desat65 (SEQ ID NO: 137), Desat27 (SEQ ID NO: 138), and Desat73, preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17.

In one embodiment, the Ncb5or is DmNcb5or (SEQ ID NO: 112), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16,

FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is DgNcb5or).

5 In one embodiment, the Ncb5or is HsNcb5or (SEQ ID NO: 113), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is
10 DgNcb5or).

In one embodiment, the Ncb5or is SlitNcb5or (SEQ ID NO: 114), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16,
15 FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is DgNcb5or).

In one embodiment, the Ncb5or is CpoNcb5or1 (SEQ ID NO: 124), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is
20 DgNcb5or).

25 In one embodiment, the Ncb5or is CpNcb5or (SEQ ID NO: 182), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is
30 DgNcb5or).

In one embodiment, the Ncb5or is AseNcb5or (SEQ ID NO: 183), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or),

preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is DgNcb5or).

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In one embodiment, the Ncb5or is BterNcb5or (SEQ ID NO: 184), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is DgNcb5or).

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In one embodiment, the Ncb5or is LboNcb5or (SEQ ID NO: 185), the FAR is selected from the group of FARs listed above (in the context of an Ncb5or which is DgNcb5or), preferably the FAR is selected from the group consisting of FAR1, FAR15, FAR16, FAR12, FAR6, FAR8, FAR18, FAR38, and FAR17, and the desaturase is selected from the group of desaturases listed above (in the context of an Ncb5or which is DgNcb5or).

15

20 *Cell*

The present invention provides a cell which has been modified or engineered to produce desaturated and/or saturated compounds, in particular to produce desaturated and/or saturated fatty alcohols; desaturated and/or saturated fatty alcohol acetates; and/or desaturated and/or saturated fatty aldehydes. Some of these are components of pheromones, in particular of moth pheromones. The cell disclosed herein thus provides an improved platform for environment-friendly moth pheromone production.

25

In one embodiment, the cell described herein is capable of producing a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and/or a saturated fatty alcohol acetate have a carbon chain length of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22. In preferred embodiments, the carbon chain has a length of 11, 12, 13, 14, 15, 16, 17 or 18.

30

Accordingly, one embodiment of the present invention provides a cell expressing

- i) a first enzyme or group of enzymes capable of converting a fatty-acyl CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and
- 5 ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);
- whereby the cell is capable of producing the compound with a higher titer compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.
- 10 In one embodiment, the first enzyme or group of enzymes consists of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA, whereby the cell is capable of producing a desaturated fatty acyl-CoA with a higher titer compared to a cell expressing said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.
- 15 In one embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) capable of converting a fatty acyl-CoA to a saturated fatty alcohol, whereby the cell is capable of producing a saturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR but no heterologous Ncb5or
- 20 when cultivated in the same conditions.
- In one embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol, whereby the cell is capable of producing a
- 25 desaturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR and said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.
- In one embodiment, the cell further expresses an acetyltransferase capable of
- 30 converting a desaturated or a saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively, whereby the cell is capable of producing a desaturated or a saturated fatty alcohol acetate with a higher titer compared to a cell expressing the first group of enzymes and the acetyltransferase but no heterologous Ncb5or when cultivated in the same conditions.

The cell may express any of the combinations of Ncb5or and first enzyme or group of enzymes, in particular any desaturase or FAR, described herein.

In one embodiment, the cell expresses a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) selected from the group consisting SEQ ID NOs: 111 to 114, SEQ ID NO: 124 and SEQ ID NOs: 182 to 185, a heterologous desaturase selected from the group consisting of SEQ ID NOs: 1 to 38 and SEQ ID NO: 126 to 139, and a heterologous fatty acyl CoA reductase (FAR) selected from the group consisting of SEQ ID NOs: 77 to 93 and SEQ ID NO: 154-167; for example a desaturase from *Spodoptera litura* (Desat38) as set forth in SEQ ID NO: 32, and a fatty acyl CoA reductase (FAR) from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83; or a desaturase from *Lobesia botrana* (Desat30) as set forth in SEQ ID NO: 20, and a fatty acyl CoA reductase (FAR) from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83; or a desaturase from *Drosophila virilis* (Desat61) as set forth in SEQ ID NO: 15, and a fatty acyl CoA reductase (FAR) from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83.

In one embodiment, the cell expresses:

- a. a desaturase from *Spodoptera litura* (Desat38) as set forth in SEQ ID NO: 32;
- b. a fatty acyl CoA reductase (FAR) as described herein above, such as a *Helicoverpa armigera* FAR, for example FAR1 as set forth in SEQ ID NO: 83, or such as a FAR from *Agrotis segetum*, for example FAR12 as set forth in SEQ ID NO: 77; and
- c. an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) selected from the group consisting of an Ncb5or from *Drosophila melanogaster* such as DmNcb5or as set forth in SEQ ID NO: 112, an Ncb5or from *Spodoptera litura* such as SlitNcb5or as set forth in SEQ ID NO: 114, an Ncb5or from *Drosophila grimshawi* such as DgNcb5or as set forth in SEQ ID NO: 111, an Ncb5or from *Cydia pomonella* such as CpNcb5or as set forth in SEQ ID NO: 182, an Ncb5or from *Agrotis segetum* such as AseNcb5or as set forth in SEQ ID NO: 183, an Ncb5or from *Bombus terrestris* such as BterNcb5or as set forth in SEQ ID NO: 184, an Ncb5or from *Lobesia botrana* such as LboNcb5or as set forth in SEQ ID NO: 185, and an Ncb5or from *Homo sapiens* such as HsNcb5or as set forth in SEQ ID NO: 113,

or variants thereof having at least 60% identity thereto. In some embodiments the FAR is FAR1 and the Ncb5or is DmNcb5or or SlitNcb5or; in other embodiments the FAR is FAR12 and the Ncb5or is DmNcb5or.

5 In other embodiments the cell expresses:

- a. a desaturase from *Lobesia botrana* such as Desat30 as set forth in SEQ ID NO: 20;
 - b. a fatty acyl CoA reductase (FAR) from *Helicoverpa armigera* such as FAR1 as set forth in SEQ ID NO: 83; and
 - 10 c. an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) selected from the group consisting of an Ncb5or from *Drosophila melanogaster* such as DmNcb5or as set forth in SEQ ID NO: 112, an Ncb5or from *Spodoptera litura* such as SlitNcb5or as set forth in SEQ ID NO: 114, an Ncb5or from *Drosophila grimshawi* such as DgNcb5or as set forth in SEQ ID NO: 111,
 - 15 an Ncb5or from *Cydia pomonella* such as CpNcb5or as set forth in SEQ ID NO: 182, an Ncb5or from *Agrotis segetum* such as AseNcb5or as set forth in SEQ ID NO: 183, an Ncb5or from *Bombus terrestris* such as BterNcb5or as set forth in SEQ ID NO: 184, an Ncb5or from *Lobesia botrana* such as LboNcb5or as set forth in SEQ ID NO: 185, and an Ncb5or from *Homo sapiens* such as HsNcb5or as set forth in SEQ ID NO: 113, preferably
 - 20 DmNcb5or or SlitNcb5or,
- or variants thereof having at least 60% identity thereto.

In other embodiments the cell expresses:

- 25 a. a desaturase from *Drosophila virilis* such as Desat61 as set forth in SEQ ID NO: 15;
- b. a fatty acyl CoA reductase (FAR) from *Helicoverpa armigera* such as FAR1 as set forth in SEQ ID NO: 83; and
- 30 c. an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) selected from the group consisting of an Ncb5or from *Drosophila melanogaster* such as DmNcb5or as set forth in SEQ ID NO: 112, an Ncb5or from *Spodoptera litura* such as SlitNcb5or as set forth in SEQ ID NO: 114, an Ncb5or from *Drosophila grimshawi* such as DgNcb5or as set forth in SEQ ID NO: 111,
- 35 an Ncb5or from *Cydia pomonella* such as CpNcb5or as set forth in SEQ ID NO: 182, an Ncb5or from *Agrotis segetum* such as AseNcb5or as set forth

in SEQ ID NO: 183, an Ncb5or from *Bombus terrestris* such as BterNcb5or as set forth in SEQ ID NO: 184, an Ncb5or from *Lobesia botrana* such as LboNcb5or as set forth in SEQ ID NO: 185, and an Ncb5or from *Homo sapiens* such as HsNcb5or as set forth in SEQ ID NO: 113, preferably HsNcb5or or SlitNcb5or,
5 or variants thereof having at least 60% identity thereto.

The term "variant thereof having at least 60% identity" in relation to a given enzyme shall be understood to refer to variants having 60% identity or more to said enzyme,
10 such as at least 61% identity, such as at least 62% identity, such as at least 63% identity, such as at least 64% identity, such as at least 65% identity, such as at least 66% identity, such as at least 67% identity, such as at least 68% identity, such as at least 69% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such
15 as at least 76%, such as at least 77%, such as at least 78%, such as at least 79%, such as at least 80%, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such
20 as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to the enzyme, or more.

Fatty alcohols and fatty alcohol acetates

The cell expressing said Ncb5or and said first enzyme or group of enzymes is capable
25 of producing fatty alcohols and/or fatty alcohol acetates having a carbon chain length of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22. In preferred embodiments, the carbon chain has a length of 11, 12, 13, 14, 15, 16, 17 or 18.

Thus, provided herein is a desaturated fatty alcohol, a saturated fatty alcohol, a
30 desaturated fatty alcohol acetate, and/or a saturated fatty alcohol acetate obtainable according to the methods presented herein.

Further provided herein is the use of a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and/or a saturated fatty alcohol acetate

obtainable according to the methods presented herein. Such compounds can be used for example for monitoring the presence of pest or disrupting the presence of pest.

5 In some embodiments, the desaturated fatty alcohol is desaturated in at least one position, such as at least two positions. In other embodiments, the desaturated fatty alcohol is desaturated at position 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21. In preferred embodiments, the desaturated fatty alcohol is selected from the group of desaturated fatty alcohols consisting of (Z)-9-tetradecen-1-ol (Z9-14:OH), (Z)-9-hexadecen-1-ol (Z9-16:OH), (Z)-11-tetradecen-1-ol (Z11-14:OH), (Z)-11-
10 hexadecen-1-ol (Z11-16:OH), and codlemone (E8,E10-dodecadien-1-ol).

In some embodiments, the desaturated fatty alcohol acetate is desaturated in at least one position, such as at least two positions. In other embodiments, the desaturated fatty alcohol acetate is desaturated at position 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15,
15 16, 17, 18, 19, 20 or 21. In some embodiments the desaturated fatty alcohol acetate is E8,E10-dodecadienyl acetate.

In some embodiments, the cell is capable of further converting the desaturated fatty alcohol acetate or the saturated fatty alcohol acetate into a desaturated fatty aldehyde or a saturated fatty aldehyde, respectively, e.g. by expression of at least one alcohol
20 dehydrogenase and/or at least one fatty alcohol oxidase in said cell. The alcohol dehydrogenase and/or at the fatty alcohol oxidase may be native to the cell, or may be a heterologous alcohol dehydrogenase and/or at the fatty alcohol oxidase.

25 Thus, further provided herein is the use of a desaturated fatty aldehyde, and/or a saturated fatty aldehyde obtainable according to the methods presented herein.

Alternatively, an acetyltransferase may catalyse the conversion of a desaturated fatty alcohol or a saturated fatty alcohol produced by the cell to the corresponding
30 desaturated fatty aldehyde or saturated fatty aldehyde, either in vivo or in vitro after recovering the fatty alcohol. Conversion into a fatty aldehyde may also be done chemically.

Any of the desaturated fatty alcohols produced by the cell may further be converted
35 into the corresponding fatty alcohol acetate. In preferred embodiments, (Z)-9-

tetradecen-1-yl acetate (Z9-14:OAc), (Z)-9-hexadecen-1-yl acetate (Z9-16:OAc), (Z)-11-tetradecen-1-yl acetate (Z11-14:OAc), (Z)-11-hexadecen-1-yl acetate (Z11-16:OAc), and E8,E10-dodecadien-1-yl acetate (E8,E10-Z11:OAc).

5 In some embodiments, the product is (Z)-11-hexadecen-1-ol (Z11-16:OH). Such product can be obtained as disclosed in WO 2016/207339. For example, it may be produced by expressing a Δ 11 desaturase and a FAR in a cell, such as a yeast cell or a plant cell, preferably a yeast cell, wherein said Δ 11 desaturase is capable of converting hexadecanoyl-CoA to (Z)11-hexadecenoyl-CoA and said FAR is capable of
10 converting (Z)11-hexadecenoyl-CoA to (Z)-11-hexadecen-1-ol. In particular, the following desaturases and FARs have been found to allow production of these compounds in yeast with a high titer: *Amyelois transitella* desaturases, such as Desat16; *Spodoptera littoralis* desaturases, such as Desat20; *Spodoptera exigua* desaturases, such as Desat37; *Agrotis segetum* desaturases, such as Desat19;
15 *Trichoplusia ni* desaturases such as Desat21; *Helicoverpa armigera* FARs such as FAR1; *Heliothis subflexa* FAR such as FAR4 and *Helicoverpa assulta* FARs such as FAR6; or variants thereof having at least 60% identity thereto.

In some embodiments, the product is codlemone (E8,E10-dodecadien-1-ol). Such
20 product can be obtained as disclosed in application PCT/EP2020/086975 filed by same applicant on 18 December 2020 and entitled "Yeast cells and methods for production of E8,E10-dodecadienyl coenzyme A, codlemone and derivatives thereof". For example, E8,E10-dodecadien-1-ol can be produced in a cell, such as a yeast cell or a plant cell, preferably a yeast cell, said cell expressing at least one heterologous desaturase
25 capable of introducing one or more double bonds in a fatty acyl-CoA having a carbon chain length of 12, thereby converting said fatty acyl-CoA to a desaturated fatty acyl-CoA, wherein at least part of said desaturated fatty acyl-CoA is E8,E10-dodecadienyl coenzyme A (E8,E10-C12:CoA). In particular, the following desaturases can be expressed in yeast in order to produce codlemone with a high titer: Desat4 alone, or
30 Desat4 (SEQ ID NO: 9) and an additional heterologous desaturase such as Desat2 (SEQ ID NO: 10) or Desat1 (SEQ ID NO: 11) or variants thereof having at least 60% identity thereto. Said desaturases can advantageously be expressed with at least one of the following FARs: fatty acyl-CoA reductase is selected from the group consisting of FAR12 (SEQ ID NO: 77), FAR18 (SEQ ID NO: 78), FAR4 (SEQ ID NO: 85), FAR6

(SEQ ID NO: 84), FAR5 (SEQ ID NO: 86), FAR1 (SEQ ID NO: 83), FAR23 (SEQ ID NO: 82), or variants thereof having at least 60% identity thereto.

5 In order to improve production of desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, desaturated fatty aldehydes, or saturated fatty aldehydes as disclosed herein, for example of E8,E10-dodecadienyl coenzyme A and optionally E8,E10-dodecadien-1-ol and derivatives thereof, it may be advantageous to introduce additional modifications in the cell in order to increase availability of the required precursors. Such modifications are disclosed in
10 application PCT/EP2020/086975 filed by same applicant on 18 December 2020 and entitled "Yeast cells and methods for production of E8,E10-dodecadienyl coenzyme A, codlemone and derivatives thereof", and can be useful for production of a variety of desaturated compounds besides codlemone. For example, the cell may be further modified to express a heterologous cytochrome b5; and/or to express a heterologous
15 cytochrome b5 reductase; and/or to express a haemoglobin; and/or by inactivation of native elongase(s); and/or by inactivation of native thioesterases; and/or by inactivation or modification of activity of native fatty aldehyde dehydrogenases, fatty alcohol oxidases, peroxisome biogenesis factor and/or fatty acyl synthases; and/or by expression of a heterologous thioesterase gene; and/or by expression of a fusion
20 protein of fatty acyl synthase and of a thioesterase. In particular, expression of a heterologous cytochrome b5, of a heterologous cytochrome b5 reductase, and/or of a haemoglobin, and/or inactivation or reduction of activity of native fatty aldehyde dehydrogenases, fatty alcohol oxidase, peroxisome biogenesis facts and/or fatty acyl synthases are particularly relevant and are described in detail in application
25 PCT/EP2020/086975.

In some embodiments, particularly embodiments where the cell is a yeast cell, the cell is further modified in order to increase availability of fatty acyl-CoAs of a given chain length by chain shortening, as disclosed in WO 2020/169389. Without being bound by
30 theory, such modifications are expected to increase availability of substrates having a desired carbon chain length, in particular having a carbon chain length of 12, whereby production of desaturated fatty alcohols and optionally of desaturated fatty alcohol acetates and desaturated fatty aldehydes can be increased. This can be achieved by reducing the activity of native acyl-CoA oxidases in a microbial production cell and by

expressing specific acyl-CoA oxidases, desaturases, reductases, and acetyltransferases. Such modifications are described in detail in WO 2020/169389.

5 Any of the above modifications can be combined, i.e. the cell may comprise several of said modifications.

Fatty aldehydes

While the present disclosure provides methods for producing desaturated and saturated fatty alcohols, and desaturated and saturated fatty alcohol acetates, it may
10 be of interest to further convert said fatty alcohols to the corresponding desaturated or saturated aldehydes. Thus in some embodiments, the method may further comprise the step of converting at least part of the fatty alcohols to fatty aldehydes, thereby producing fatty aldehydes. This can be achieved by chemical methods or by further engineering of the yeast cell.

15 In some embodiments, the step of converting at least part of the fatty alcohols to the corresponding aldehydes is a step of chemical conversion. The chemical conversion is based on the oxidation of fatty alcohols to the corresponding aldehydes. Methods for performing this conversion are known in the art. Preferred methods are environmentally
20 friendly and minimize the amount of hazardous waste.

Thus in some embodiments, the chemical conversion may be metal free, avoiding toxic heavy metal based reagents such as manganese oxides, chromium oxides (Jones ox. PDC, PCC) or ruthenium compounds (TPAP, Ley-Griffith ox.). In some embodiments,
25 the conversion does not involve reactions with activated dimethyl sulfoxide such as the Swern oxidation or the Pfitzner-Moffat type. Such reactions may involve the stereotypic formation of traces of intensively smelling organic sulfur compounds such as dimethyl sulfide which can be difficult to remove from the target product.

30 In some embodiments, the method comprises a Dess-Martin reaction (Yadav et al., 2004, Meyer et al., 1994). In some embodiments, the method comprises a Copper(I)/ABNO-catalysed aerobic alcohol oxidation reaction (Steves & Stahl, 2013).

35 In other embodiments, the chemical conversion comprises the oxidation with sodium hypochlorite under aqueous/organic two phase conditions (Okada et al., 2014; Tamura

et al., 2012; Li et al., 2009). In some embodiments, the chemical oxidation can be performed with 1-chlorobenzotriazole in a medium of methylene chloride containing 25% pyridine (Ferrell and Yao, 1972).

- 5 Alternatively, the oxidation of a fatty alcohol to the corresponding fatty aldehyde can be performed enzymatically by alcohol dehydrogenases. The skilled person will know how to carry out enzymatic oxidation. For example, enzymatic oxidation can be carried out by contacting purified enzymes, cell extracts or whole cells, with the fatty alcohol.
- 10 The fatty alcohols obtainable by the cells and methods described herein can be further converted to fatty aldehydes by introducing a gene encoding an aldehyde-forming fatty acyl-CoA reductase EC 1.2.1.50 (FAR'). In this way, at least part of the fatty acyl-CoA can be converted to the corresponding fatty aldehyde by an aldehyde-forming fatty acyl-CoA reductase (FAR'). The enzymes capable of catalysing this conversion can
- 15 catalyse a reduction reaction, where the fatty acyl-CoA is reduced to a fatty aldehyde. Such enzymes are aldehyde-forming fatty acyl-CoA reductases, herein also referred to as FAR' or "aldehyde-forming FAR' ", with an EC number 1.2.1.50. They catalyse the following reaction:
- 20 $\text{Fatty acyl-CoA} + \text{NADPH} = \text{fatty aldehyde} + \text{NADP}^+ + \text{coenzyme A}.$

Yeast cell

- In some embodiments of the present invention, the cell provided herein is a yeast cell. Accordingly, one embodiment of the present invention provides a yeast cell expressing
- 25 a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or); whereby the yeast cell is capable of producing the compound with a higher titer compared to a yeast cell
- 30 expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

The yeast cell may be a non-naturally occurring yeast cell, for example a yeast cell which has been engineered to produce desaturated fatty alcohols, saturated fatty

alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs.

5 In some embodiments, the cell has been modified at the genomic level, e.g. by gene editing in the genome. The cell may also be modified by insertion of at least one nucleic acid construct such as at least one vector. The vector may be designed as is known to the skilled person to either enable integration of nucleic acid sequences in the genome, or to enable expression of a polypeptide encoded by a nucleic acid sequence comprised in the vector without genome integration.

10 The yeast cell may be of a genus selected from *Saccharomyces*, *Pichia*, *Komagataella*, *Yarrowia*, *Kluyveromyces*, *Candida*, *Rhodotorula*, *Rhodospiridium*, *Cryptococcus*, *Trichosporon* and *Lipomyces*. In a preferred embodiment, the genus is *Saccharomyces* or *Yarrowia*, most preferably the genus is *Yarrowia*.

15 The yeast cell may be of a species selected from *Saccharomyces cerevisiae*, *Saccharomyces boulardi*, *Pichia pastoris*, *Komagataella phaffii*, *Komagataella pastoris*, *Komagataella pseudopastoris*, *Kluyveromyces marxianus*, *Candida tropicalis*, *Cryptococcus albidus*, *Lipomyces lipofera*, *Lipomyces starkeyi*, *Rhodospiridium*
20 *toruloides*, *Rhodotorula glutinis*, *Trichosporon pullulan* and *Yarrowia lipolytica*. In preferred embodiments, the yeast cell is a *Saccharomyces cerevisiae* cell or a *Yarrowia lipolytica* cell, most preferably the yeast cell is a *Yarrowia lipolytica* cell.

25 The yeast cell to be modified, which will also be referred to as the host cell, may express native enzymes which are of the same class as the enzymes which are necessary for the production of desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs. In some cases, however, such native enzymes may have a negative impact on the titer of desaturated fatty alcohols, saturated fatty alcohols, desaturated
30 fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs which can be obtained; the native enzymes may thus be inactivated by methods known in the art, such as gene editing. For example, the genes encoding the native enzymes having a negative impact on the titer may be deleted or mutated so as to lead to total or partial loss of activity of the native enzyme.

35

In some embodiments, the yeast cell has reduced activity of one or proteins as disclosed in WO 2018/109163 and in European patent 3555268. For example, the yeast cell may have a mutation resulting in reduced activity (i.e. downregulation) of Pex10, Hfd1, Hfd4, Fao1 and/or GPAT. Preferably, the yeast cell has at least one
5 mutation resulting in reduced activity of at least Fao1 and one or more of Hfd1, Hfd4, Pex10 and/or GPAT. Such mutations may increase the production of desaturated fatty alcohol and/or desaturated fatty alcohol acetate in a yeast cell expressing a heterologous desaturase and a heterologous fatty acyl-CoA reductase.

10 Thus, provided here is a yeast cell expressing a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and a heterologous NAD(P)H cytochrome b5
15 oxidoreductase (Ncb5or); whereby the yeast cell is capable of producing the compound with a higher titer compared to a yeast cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

The first enzyme or group of enzymes may be a desaturase as defined in the section "Desaturase"; a FAR as defined in the section "Fatty acyl-CoA reductase"; a
20 desaturase and a FAR desaturase as defined in the sections "Desaturase" and "Fatty acyl-CoA reductase", respectively. The Ncb5or may be as defined in the section "NAD(P)H cytochrome b5 oxidoreductase". The yeast cell may express a heterologous Ncb5or and a heterologous desaturase; a heterologous FAR; or a heterologous FAR and a heterologous desaturase as disclosed in the section "Cell".

25 In some embodiments, the genes encoding said desaturase, FAR and/or Ncb5or has been codon optimized for said yeast cell. In other embodiments, the genes encoding said desaturase, FAR and/or Ncb5or are under control of an inducible promoter. In some embodiments, the genes encoding said desaturase, FAR and/or Ncb5or are
30 present in high copy number, and/or they are each independently comprised within the genome of the yeast cell or within a vector comprised in the yeast cell.

In some embodiments, the yeast cell comprises a system of vectors, as described in the section "Nucleic acid".

35

The yeast cell according to the present invention may be comprised in a fermentation broth, a fermentation system, and/or a catalytic system. In other words, a fermentation broth, a fermentation system and/or a catalytic system may comprise the yeast cell according to the present invention.

5

Plant cell

In some embodiments of the present invention, the cell provided herein is a plant cell. Accordingly, one embodiment of the present invention provides a plant cell expressing a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA; and a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or); whereby the plant cell is capable of producing the compound with a higher titer compared to a plant cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

10
15

The plant cell may be a non-naturally occurring plant cell, for example a plant cell which has been engineered to produce desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs.

20

In some embodiments, the plant cell has been modified at the genomic level, e.g. by gene editing in the genome. The plant cell may also be modified by insertion of at least one nucleic acid construct such as at least one vector. The vector may be designed as is known to the skilled person to either enable integration of nucleic acid sequences in the genome, or to enable expression of a polypeptide encoded by a nucleic acid sequence comprised in the vector without genome integration. For example, the plant cell may be modified using horizontal gene transfer, a gene gun, and/or other techniques known in the art.

25

30

In some embodiments, the plant cell is from a genus selected from the group consisting of *Nicotiana* and *Camelina*. In some embodiments, the plant cell is from a species selected from the group consisting of *Nicotiana tabacum*, *Nicotiana benthamiana*, and *Camelina sativa*.

35

The plant cell to be modified, which will also be referred to as the host cell, may express native enzymes which are of the same class as the enzymes which are necessary for the production of desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs. In some cases, however, such native enzymes may have a negative impact on the titer of desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, saturated fatty alcohol acetates, and a desaturated fatty acyl-CoAs which can be obtained; the native enzymes may thus be inactivated by methods known in the art, such as gene editing. For example, the genes encoding the native enzymes having a negative impact on the titer may be deleted or mutated so as to lead to total or partial loss of activity of the native enzyme.

The plant cell may be part of a plant, such as a genetically modified plant. In other words, the plant cell may be part of a transgenic plant. Transgenic plants are plants expressing a transgene, i.e. plants which have been genetically engineered. Plant genomes can be engineered by physical methods or by use of *Agrobacterium* for the delivery of sequences.

A gene gun, or a biolistic particle delivery system, is an example of a physical plant genetic engineering method. The gene gun may be used to deliver exogenous DNA, RNA or protein to plant cells. By coating particles with a gene of interest and firing these micro-projectiles into cells using mechanical force, an integration of desired genetic information can be induced into cells. The gene gun is able to transform almost any type of plant cell and is not limited to transformation of the nucleus; it can also transform organelles including plastids and mitochondria.

Agrobacterium is a genus of Gram-negative bacteria that uses horizontal gene transfer to cause tumours in plants. *Agrobacterium* well known for its ability to transfer DNA between itself and plants, and has for this reason become an important tool for genetic engineering of plants. Genomes of plants can be engineered by the use of *Agrobacterium* for the delivery of sequences hosted in transfer-binary vectors (T-binary vectors). The transformation with *Agrobacterium* can be achieved in multiple ways. Protoplasts or leaf-discs can be incubated with the *Agrobacterium*, and whole plants generated as described below. In agroinfiltration, the *Agrobacterium* may be injected directly into the leaf tissue of a plant.

Many plants are pluripotent, meaning that a single cell from a mature plant can be harvested and used to form a new plant. This can be utilized when making transgenic plants. Cells which have been successfully transformed in an adult plant can be
5 harvested and grown in plant tissue culture to generate a new plant, where the genetic modification is present in every cell of said plant.

The plant of the present disclosure is not a naturally occurring plant. Preferably, the plant disclosed herein is not obtained by essentially biological methods, but is generally
10 obtained by targeted genome editing methods, as is known in the art.

Thus, provided here is a plant cell expressing a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a
15 desaturated fatty acyl-CoA; and a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or); whereby the plant cell is capable of producing the compound with a higher titer compared to a plant cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.

20 The first enzyme or group of enzymes may be a desaturase as defined in the section "Desaturase"; a FAR as defined in the section "Fatty acyl-CoA reductase"; a desaturase and a FAR desaturase as defined in the sections "Desaturase" and "Fatty acyl-CoA reductase", respectively. The Ncb5or may be as defined in the section NAD(P)H cytochrome b5 oxidoreductase". The plant cell may express a heterologous
25 Ncb5or and a heterologous desaturase; a heterologous FAR; or a heterologous FAR and a heterologous desaturase as disclosed in the section "Cell".

In some embodiments, the genes encoding said desaturase, FAR and/or Ncb5or has been codon optimized for said plant cell. In other embodiments, the genes encoding
30 said desaturase, FAR and/or Ncb5or are under control of an inducible promoter. In some embodiments, the genes encoding said desaturase, FAR and/or Ncb5or are present in high copy number, and/or they are each independently comprised within the genome of the plant cell or within a vector comprised in the plant cell.

In some embodiments, the plant cell comprises a system of vectors, as described in the section "Nucleic acid".

5 *Method for production of desaturated fatty acyl CoAs, desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, and/or saturated fatty alcohol acetates*

Provided herein is a method for production of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA in a cell, said method comprising the steps of:

- 10 a. providing a cell and incubating said cell in a medium; and
 b. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
 c. expressing in said cell an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);
15 d. optionally, recovering said compound.

In some embodiments, the methods presented herein yields said desaturated fatty alcohol, and optionally said fatty alcohol acetate and/or fatty acid with a titer of at least 1 mg/L, such as at least 1.5 mg/L, such as at least 5 mg/L, such as at least 10 mg/L,
20 such as at least 25 mg/L, such as at least 50 mg/L, such as at least 100 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at least 750 mg/L, such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L, such as at least 4 g/L, such as at least 5 g/L, such as at least 6 g/L, such as at least 7 g/L, such as at least 8 g/L, such as at least 9 g/L, such as at least 10 g/L, such as at least 11 g/L, such as at least 12
25 g/L, such as at least 13 g/L, such as at least 14 g/L, such as at least 15 g/L, such as at least 16 g/L, such as at least 17 g/L, such as at least 18 g/L, such as at least 19 g/L, such as at least 20 g/L, such as at least 25 g/L, such as at least 30 g/L, such as at least 35 g/L, such as at least 40 g/L, such as at least 45 g/L, such as at least 50 g/L, such as at least 55 g/L, such as at least 60 g/L, such as at least 65 g/L, such as at least 70 g/L,
30 such as at least 75 g/L, such as at least 80 g/L, such as at least 85 g/L, such as at least 90 g/L, such as at least 95 g/L, such as at least 100 g/L, such as at least 125 g/L, such as at least 150 g/L, such as at least 175 g/L, such as at least 200 g/L, or more.

Further provided herein is a method of increasing the titer of a compound selected from
35 a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol

acetate, a desaturated fatty acid and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:

- a. expressing in said cell a first enzyme or group of enzymes capable of
5 converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- b. expressing in said cell an NAD(P)H cytochrome b5 reductase (Ncb5or), thereby increasing the titer of said compound compared to the titer from a cell not expressing said Ncb5or in the same conditions;
- 10 c. optionally, recovering said compound.

In other words, provided herein is a method to increase the production of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a desaturated fatty acid and a desaturated fatty acyl-CoA in a cell,
15 wherein said cell expresses a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to any of said compounds, thereby converting at least part of said fatty acyl-CoA to any of said said compounds; and expressing in said cell an NAD(P)H cytochrome b5 reductase (Ncb5or); wherein the production of said compound in said cell is increased compared to the production of said compound in said cell which
20 expresses the same enzyme or first group of enzymes, but not an Ncb5or, wherein said cells are cultivated under the same conditions.

Also disclosed herein is a method for increasing the purity of a compound selected from a a desaturated fatty alcohol, a desaturated fatty acid and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or
25 capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:

- a. expressing in said cell a first enzyme or group of enzymes capable of
30 converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- b. expressing in said cell an Ncb5or, thereby increasing the production of said compound compared to the production from a cell not expressing said Ncb5or in the same conditions;

wherein the purity of said compound is the ratio or percentage of said compound in
35 relation to all compounds within the same compound group produced by the cell, such

as the percentage of said desaturated fatty alcohol in relation to all desaturated fatty alcohols produced by the cell, such as the percentage of desaturated fatty acid in relation to all fatty acids produced by the cell, and/or such as the percentage of desaturated fatty acyl-CoA in relation to all fatty acyl-CoA produced by the cell.

5

The purity of desaturated fatty alcohol, desaturated fatty acid and/or desaturated fatty acyl-CoA may be increased by at least 3% compared to the purity of the same compound obtained from a cell not expressing said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such as at least 55%, such as at least 60%, such as at least 70%, such as at least 80%, such as at least 90%, such as at least 100%, such as at least 150%, such as at least 200%, such as at least 250%.

10

15

In one embodiment, the first enzyme or group of enzymes consists of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA and wherein said compound is a desaturated fatty acyl-CoA. Fatty acyl-CoAs do not accumulate in the cell but their presence can be determined by determining the presence of the corresponding fatty acid.

20

In one embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) capable of converting a fatty acyl-CoA to a saturated fatty alcohol and wherein said compound is a saturated fatty alcohol.

25

In one embodiment, the first enzyme or group of enzymes consists of one or more fatty acyl reductase (FAR) and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol and wherein said compound is a desaturated fatty alcohol.

30

In one embodiment, the compound is a desaturated or a saturated fatty alcohol and wherein the method further comprises the step of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively.

In one embodiment, the conversion of the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate is performed in vitro.

5 In one embodiment, the conversion of the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate is performed in vivo by further expressing in the cell an acetyltransferase capable of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively.

10 In one embodiment, compound is a saturated fatty alcohol or a desaturated fatty alcohol, and wherein the method further comprises a step of converting the saturated fatty alcohol or the desaturated fatty alcohol to a saturated fatty aldehyde or to a desaturated fatty aldehyde, respectively.

15 In one embodiment, the conversion to an aldehyde is a chemical or an enzymatic conversion.

In some embodiments, the cell is a yeast cell as described in the section "Yeast cell". In some embodiments, the cell is a plant cell as described in the section "Plant cell".

20 The desaturase, FAR and Ncb5or may be as described in the sections "Desaturase", "Fatty acyl-CoA reductase" and "NAD(P)H cytochrome b5 oxidoreductase", respectively.

25 In some embodiments, the total titer of desaturated fatty alcohols and optionally the total titer of desaturated fatty alcohol acetates and/or of desaturated fatty acids is increased. In other embodiments, the total titer of saturated fatty alcohols and optionally the total titer of saturated fatty alcohol acetates and/or of desaturated fatty acids is increased.

30 In some embodiments, the titer of desaturated fatty alcohol is increased at least 3% compared to the titer from a cell such as a yeast cell or a plant cell not expressing said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as
35 at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such

as at least 55%, such as at least 60%, such as at least 70%, such as at least 80%,
such as at least 90%, such as at least 100%, such as at least 150%, such as at least
200%, such as at least 250%.

5 In some embodiments, the titer of saturated fatty alcohol acetate is increased at least
3% compared to the titer from a cell such as a yeast cell or a plant cell not expressing
said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as
at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such
as at least 35%, such as at least 40%, such as at least 45%, such as at least 50%,
10 such as at least 55%, such as at least 60%, such as at least 70%, such as at least
80%, such as at least 90%, such as at least 100%, such as at least 150%, such as at
least 200%, such as at least 250%.

In some embodiments, the titer of saturated fatty alcohol acid is increased at least 3%
15 compared to the titer from a cell such as a yeast cell or a plant cell not expressing said
Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at
least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as
at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such
as at least 55%, such as at least 60%, such as at least 70%, such as at least 80%,
20 such as at least 90%, such as at least 100%, such as at least 150%, such as at least
200%, such as at least 250%.

Further provided herein is a method for producing at least 1 mg/L of desaturated fatty
alcohol, saturated fatty alcohol, desaturated fatty alcohol acetate, saturated fatty
25 alcohol acetate, saturated fatty acid, desaturated fatty acid, desaturated fatty aldehyde,
and/or saturated fatty aldehyde, such as at least 1.5 mg/L, such as at least 5 mg/L,
such as at least 10 mg/L, such as at least 25 mg/L, such as at least 50 mg/L, such as
at least 100 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at
least 750 mg/L, such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L,
30 such as at least 4 g/L, such as at least 5 g/L, such as at least 6 g/L, such as at least 7
g/L, such as at least 8 g/L, such as at least 9 g/L, such as at least 10 g/L, such as at
least 11 g/L, such as at least 12 g/L, such as at least 13 g/L, such as at least 14 g/L,
such as at least 15 g/L, such as at least 16 g/L, such as at least 17 g/L, such as at least
18 g/L, such as at least 19 g/L, such as at least 20 g/L, such as at least 25 g/L, such as

at least 30 g/L, such as at least 35 g/L, such as at least 40 g/L, such as at least 45 g/L, such as at least 50 g/L, or more.

Methods for determining the titer are known in the art.

5

Any of the methods disclosed herein may further comprise a step of converting the desaturated or the saturated fatty alcohol acetate into a desaturated or a saturated fatty aldehyde. This can be done as detailed above, e.g. by expression of at least one alcohol dehydrogenase and/or at least one fatty alcohol oxidase in said cell. The
10 alcohol dehydrogenase and/or at the fatty alcohol oxidase may be native to the cell, or may be a heterologous alcohol dehydrogenase and/or at the fatty alcohol oxidase.

Any of the methods disclosed herein may further comprise a step of converting the desaturated or saturated fatty alcohol produced by the cell to the corresponding
15 saturated or desaturated fatty aldehyde, either in vivo or in vitro after recovering the fatty alcohol. Conversion into a desaturated or saturated fatty aldehyde may also be done chemically.

In some embodiments, the cell such as a yeast cell or a plant cell is further modified in
20 order to increase availability of fatty acyl-CoAs of a given chain length by chain shortening, as disclosed in WO 2020/169389. Without being bound by theory, such modifications are expected to increase availability of substrates having a desired carbon chain length, in particular having a carbon chain length of 12, whereby production of desaturated fatty alcohols and optionally of desaturated fatty alcohol
25 acetates and desaturated fatty aldehydes can be increased. This can be achieved by reducing the activity of native acyl-CoA oxidases in a microbial production cell and by expressing specific acyl-CoA oxidases, desaturases, reductases, and acetyltransferases. Such modifications are described in detail in WO 2020/169389.

30 Other relevant modifications are available to the skilled person, some of which are detailed herein above in the section "Fatty alcohols and fatty alcohol acetates".

Methods for increasing the activity of a desaturase and/or a fatty acyl-CoA reductase

Provided herein is a method for increasing the activity of at least one enzyme selected from the group consisting of desaturases and fatty acyl CoA reductases (FAR), said method comprising the steps of:

- 5 a. providing a desaturase capable of introducing at least one double bond in a fatty acyl-CoA, thereby converting at least part of said fatty acyl-CoA to a desaturated fatty-acyl-CoA; and/or
- b. providing a fatty acyl CoA reductase (FAR) capable of converting at least part of said desaturated fatty acyl-CoA to a desaturated fatty alcohol, thereby
- 10 producing said desaturated fatty alcohol; and
- c. contacting said desaturase and/or FAR with an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or), thereby increasing the activity of said desaturase and/or FAR compared to the activity of said desaturase and/or FAR in the
- absence of said Ncb5or, wherein the activity is measured under the same
- 15 conditions;

wherein the increase in activity is measured by measuring the concentration of product formed by the desaturase and/or the FAR.

20 In some embodiments, the method is performed in vitro. In other embodiments, the method is performed in vivo. In some embodiments, the method is performed in a yeast cell, for example as described herein in the section "Yeast cell" or in a plant cell as described herein in the section "Plant cell".

25 The method may increase the concentration of a specific desaturated fatty alcohol, a specific saturated fatty alcohol, a specific desaturated fatty alcohol acetate and/or a specific desaturated fatty acid, a specific desaturated fatty alcohol acetate, and/or the total concentration of all desaturated fatty alcohols and/or all desaturated fatty alcohol acetates, and/or the total concentration of all saturated fatty alcohols and/or all saturated fatty alcohol acetates.

30 Any of the methods disclosed herein may further comprise a step of converting the saturated fatty alcohol or the desaturated fatty alcohol to a saturated fatty aldehyde or to a desaturated fatty aldehyde, respectively. This can be done as detailed above, e.g. by expression of at least one alcohol dehydrogenase and/or at least one fatty alcohol

35 oxidase in said cell. The alcohol dehydrogenase and/or the fatty alcohol oxidase may

be native to the cell, or may be a heterologous alcohol dehydrogenase and/or at the fatty alcohol oxidase.

5 Any of the methods disclosed herein may further comprise a step of converting the desaturated or saturated fatty alcohol produced by the cell to the corresponding desaturated or saturated fatty aldehyde, either in vivo or in vitro after recovering the fatty alcohol. Conversion into a desaturated or saturated fatty aldehyde may also be done chemically.

10 In some embodiments, concentration is increased at least 3% compared to the concentration in an assay performed in the absence of Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such as at least 55%, such as at
15 least 60%, such as at least 70%, such as at least 80%, such as at least 90%, such as at least 100%, such as at least 150%, such as at least 200%, such as at least 250%.

Methods to determine whether an Ncb5or increases the activity of a desaturase and/or a FAR are known in the art. For example, whether a given Ncb5or increases the
20 activity of a desaturase can be determined by incubating in a suitable solution (i) said desaturase, said Ncb5or and the fatty acyl-CoA substrate for said desaturase, and (ii) said desaturase and the fatty acyl-CoA substrate for said desaturase. After 1 hour of incubation under the same conditions, the amount (concentration) of product, i.e. the amount of desaturated fatty-acyl CoA generated by the desaturase, can be determined
25 by GC-MS. If a higher concentration of products is obtained from the solution comprising both the desaturase and the Ncb5or, it shows that said Ncb5or increases the activity of said desaturase.

30 Accordingly, herein is also provided the use of an enzyme having Ncb5or activity to increase the activity of a different enzyme or group of enzymes, such as membrane-bound enzyme or group of enzymes.

Recovery

It may be desirable to recover the products obtained by the methods disclosed herein.
35 Thus the present methods may comprise a further step of recovering the desaturated

fatty alcohol, the saturated fatty alcohol, the desaturated fatty alcohol acetate, the saturated fatty alcohol acetate, the desaturated fatty aldehyde, and/or the saturated fatty aldehyde produced by the present yeast cell.

5 In some embodiments, the method comprises a step of recovering the desaturated fatty alcohols and/or the saturated fatty alcohols. In other embodiments, the method comprises a step of recovering the desaturated fatty alcohol acetates and/or the saturated fatty alcohol acetates.

10 Methods for recovering the products obtained by the present invention are known in the art and may comprise an extraction with a hydrophobic solvent such as decane, hexane or a vegetable oil.

The recovered products may be modified further, for example may the desaturated
15 fatty alcohols and/or the saturated fatty alcohols be converted to the corresponding desaturated fatty aldehydes and/or the saturated fatty aldehydes as described herein above. In embodiments where desaturated fatty aldehydes and/or saturated fatty aldehydes are directly produced in the culture medium, e.g. in vivo or by contacting the cells with the relevant enzymes, the desaturated fatty aldehydes and/or the saturated
20 fatty aldehydes may also be recovered.

As described in application PCT/EP2020/076351 filed by same applicant on 22 September 2020 and entitled "Improved methods for production, recovery and secretion of hydrophobic compounds in a fermentation", when a fermentation system is
25 used to cultivate the cell, in particular a yeast cell, which is capable of producing desaturated fatty alcohols, desaturated fatty alcohol acetates and/or desaturated fatty aldehydes, the addition of an extractant to the culture medium may further increase titers and extracellular secretion. In some embodiments, the medium comprises an extractant in an amount equal to or greater than its cloud concentration in an aqueous
30 solution, wherein the extractant a non-ionic surfactant such as an antifoaming agent, preferably a polyethoxylated surfactant selected from: a polyethylene polypropylene glycol, a mixture of polyether dispersions, an antifoaming agent comprising polyethylene glycol monostearate such as simethicone and ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agents and combinations thereof. In
35 some embodiments:

- the non-ionic surfactant is an ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agent, such as C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate (CAS number 68002-96-0), and wherein the culture medium comprises at least 1% vol/vol of C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate, such as at least 1.5%, such as at least 2%, such as at least 2.5%, such as at least 3%, such as at least 3.5%, such as at least 4%, such as at least 5%, such as at least 6%, such as at least 7%, such as at least 8%, such as at least 9%, such as at least 10%, such as at least 12.5%, such as at least 15%, such as at least 17.5%, such as at least 20%, such as at least 22.5%, such as at least 25%, such as at least 27.5%, such as at least 30% vol/vol C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate, or more,
- the non-ionic surfactant is a polyethylene polypropylene glycol, for example Kolliphor® P407 (CAS number 9003-11-6), and wherein the culture medium comprises at least 10% vol/vol of polyethylene polypropylene glycol such as Kolliphor® P407, such as at least 11% vol/vol, such as at least 12% vol/vol, such as at least 13% vol/vol, such as at least 14% vol/vol, such as at least 15% vol/vol, such as at least 16% vol/vol, such as at least 17% vol/vol, such as at least 18% vol/vol, such as at least 19% vol/vol, such as at least 20% vol/vol, such as at least 25% vol/vol, such as at least 30% vol/vol, such as at least 35% vol/vol of polyethylene polypropylene glycol such as Kolliphor® P407, or more,
- the non-ionic surfactant is a mixture of polyether dispersions, such as antifoam 204, and wherein the culture medium comprises at least 1% vol/vol of a mixture of polyether dispersions such as antifoam 204, such as at least 1.5%, such as at least 2%, such as at least 2.5%, such as at least 3%, such as at least 3.5%, such as at least 4%, such as at least 5%, such as at least 6%, such as at least 7%, such as at least 8%, such as at least 9%, such as at least 10%, such as at least 12.5%, such as at least 15%, such as at least 17.5%, such as at least 20%, such as at least 22.5%, such as at least 25%, such as at least 27.5%, such as at least 30% vol/vol of a mixture of polyether dispersions such as antifoam 204, or more; and/or
- the non-ionic surfactant is a non-ionic surfactant comprising polyethylene glycol monostearate such as simethicone, and wherein the culture medium comprises at least 1% vol/vol of polyethylene glycol monostearate or simethicone, such as at least 1.5%, such as at least 2%, such as at least 2.5%, such as at least 3%, such as at least 3.5%, such as at least 4%, such as at least 5%, such as at

least 6%, such as at least 7%, such as at least 8%, such as at least 9%, such as at least 10%, such as at least 12.5%, such as at least 15%, such as at least 17.5%, such as at least 20%, such as at least 22.5%, such as at least 25%, such as at least 27.5%, such as at least 30% vol/vol polyethylene glycol monostearate or simethicone, or more.

In other embodiments, the culture medium comprises the extractant in an amount greater than its cloud concentration by at least 50%, such as at least 100%, such as at least 150%, such as at least 200%, such as at least 250%, such as at least 300%, such as at least 350%, such as at least 400%, such as at least 500%, such as at least 750%, such as at least 1000%, or more, and/or wherein the culture medium comprises the extractant in an amount at least 2-fold its cloud concentration, such as at least 3-fold its cloud concentration, such as at least 4-fold its cloud concentration, such as at least 5-fold its cloud concentration, such as at least 6-fold its cloud concentration, such as at least 7-fold its cloud concentration, such as at least 8-fold its cloud concentration, such as at least 9-fold its cloud concentration, such as at least 10-fold its cloud concentration, such as at least 12.5-fold its cloud concentration, such as at least 15-fold its cloud concentration, such as at least 17.5-fold its cloud concentration, such as at least 20-fold its cloud concentration, such as at least 25-fold its cloud concentration, such as at least 30-fold its cloud concentration.

The recovered products, i.e. the desaturated fatty alcohols, the saturated fatty alcohols, the desaturated fatty alcohol acetates, and/or the saturated fatty alcohol acetates, may also be formulated into a pheromone composition, such as described in the section "Pheromone composition". The composition may further comprise one or more additional compounds such as a liquid or solid carrier or substrate. Fatty aldehydes obtained from said fatty alcohols may also be comprised in such compositions.

Fatty acids can be recovered from plants by methods known in the art, e.g. after homogenisation of the leaves and recovery of the lipids by methods known in the art. The recovered lipids are hydrolyzed into free fatty acids and esterified to fatty acid alkyl ester, followed by a reduction to either fatty alcohols or fatty aldehydes.

Nucleic acid

It will be understood that throughout the present invention, the term 'nucleic acid encoding an activity' shall refer to a nucleic acid molecule capable of encoding a peptide, a protein or a fragment thereof having said activity. Such nucleic acid molecules may be open reading frames or genes or fragments thereof. A nucleic acid construct may also be a group of nucleic acid molecules, which together may encode several peptides, proteins or fragments thereof having an activity of interest. The term 'activity' or 'activity of interest' may in particular refer to one of the following activities: a desaturase as described herein, a fatty acyl-CoA reductase as described herein, and/or an NAD(P)H cytochrome b5 reductase (Ncb5or) as described herein. The nature of the one or more activity of interest will depend on the nature of the desired product one wishes to obtain with the present methods.

A system of nucleic acid constructs comprising nucleic acids encoding an NAD(P)H cytochrome b5 oxidoreductase (Ncb5or) and:

- a. a desaturase capable of introducing at least one double bond in a fatty acyl-CoA; and/or
- b. a fatty acyl CoA reductase (FAR) capable of converting at least part of a desaturated fatty acyl-CoA to a desaturated fatty alcohol.

In some embodiments, the desaturase is encoded by any one of the sequences set forth in SEQ ID NO: 39 to 76 and SEQ ID NOs: 140 to 153, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.

In some embodiments, the fatty acyl CoA reductase (FAR) is encoded by any one of the sequences set forth in SEQ ID NO: 94 to 110 and SEQ ID NOs: 168 to 181, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.

In some embodiments, Ncb5or is encoded by any one of the sequences set forth in SEQ ID NO: 115 to 118, SEQ ID NO: 125 and SEQ ID NOs: 186 to 189, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.

The system disclosed herein may further comprise all elements required for expression of nucleic acids in cell, such as in a yeast cell or a plant. Such elements include but are not limited to introns and regulatory elements such as promoters, terminators, 5'UTRs, enhancers and silencers.

Kit

Provided herein is a kit of parts for performing the present methods. The kit of parts may comprise an organism "ready to use" as described herein. In one embodiment, the organism is a yeast cell as described in the section "Yeast cell". In one embodiment, the yeast cell is a *Yarrowia* cell, such as a *Yarrowia lipolytica* cell. In one embodiment, the organism is a plant cell as described in the section "Plant cell". In one embodiment the plant cell is a tobacco plant cell.

In one embodiment, the kit of parts comprises a nucleic acid construct encoding the activities of interest to be introduced in the organism, such as the system of nucleic acids described in the section "Nucleic acid" herein. The nucleic acid construct may be provided as a plurality of nucleic acid constructs, such as a plurality of vectors, wherein each vector encodes one or several of the desired activities.

The kit of parts may optionally comprise the cell to be modified.

The kit of parts may also comprise instructions for use.

In some embodiments, the kit of parts comprises all or a combination of the above.

Pheromone composition

- The present invention thus provides compounds, in particular desaturated fatty alcohols, saturated fatty alcohols, desaturated fatty alcohol acetates, and saturated fatty alcohol acetates, as well as derivatives thereof such as desaturated fatty aldehydes and saturated fatty aldehydes, and their use. In particular, the desaturated compounds obtainable using the present cells and methods are useful as components of pheromone compositions. Such pheromone compositions may be useful for integrated pest management. They can be used as is known in the art for e.g. mating disruption.
- Thus, the desaturated fatty alcohols, the desaturated fatty alcohol acetate, and the desaturated fatty aldehydes obtainable by the present methods or using the present cells, such as yeast cell or plant cell, may be formulated in a pheromone composition.
- Such pheromone compositions may be used as integrated pest management products, which can be used in a method of monitoring the presence of pest or in a method of disrupting the mating of pest.
- Thus, provided herein is a method for monitoring the presence of pest or disrupting the mating of pest, said method comprising the steps of:
- producing a desaturated fatty alcohol, a desaturated fatty alcohol acetate, and/or a desaturated fatty aldehyde according to any of the methods disclosed herein; and
 - formulating said fatty alcohol, fatty alcohol acetate, and/or fatty aldehyde as a pheromone composition; and
 - employing said pheromone composition as an integrated pest management composition.
- Pheromone compositions as disclosed herein may be used as biopesticides. Such compositions can be sprayed or dispensed on a culture, in a field or in an orchard. They can also, as is known in the art, be soaked e.g. onto a rubber septa, or mixed with other components. In one embodiment, said compositions are placed in a device, such as a pheromone dispenser, which diffuses the pheromone composition. The dispenser may for example release pheromones at a constant, pre-adjustable, rate.
- This can result in mating disruption, thereby preventing pest reproduction, or it can be

used in combination with a trapping device to entrap the pests. Non-limiting examples of pests against which the present pheromone compositions can be used are: cotton bollworm (*Helicoverpa armigera*), striped stemborer (*Chilo suppressalis*), diamond back moth (*Plutella xylostella*), cabbage moth (*Mamestra brassicae*), large cabbage-heart caterpillar (*Crocidolomia binotalis*), European corn stalk borer (*Sesamia nonagrioides*),
5 curren clearwing (*Synanthedon tipuliformis*) and artichoke plume moth (*Platyptilia carduidactyla*). Accordingly, use of the present compositions on a culture can lead to increased crop yield, with substantially no environmental impact.

10 The relative amounts of fatty alcohols and fatty alcohol acetates in the present pheromone compositions may vary depending on the nature of the crop and/or of the pest to be controlled; geographical variations may also exist. Determining the optimal relative amounts may thus require routine optimisation. The pheromone compositions may also comprise fatty aldehydes.

15 Examples of compositions used as repellents can be found in Kehat & Dunkelblum (1993) for *H. armigera*; in Alfaro et al. (2009) for *C. suppressalis*; in Eizaguirre et al. (2002) for *S. nonagrioides*; in Wu et al. (2012) for *P. xylostella*; and in Bari et al. (2003) for *P. carduidactyla*.

20 In some embodiments, the pheromone composition may further comprise one or more additional compounds such as a liquid or solid carrier or substrate. For example, suitable carriers or substrate include vegetable oils, refined mineral oils or fractions thereof, rubbers, plastics, silica, diatomaceous earth, wax matrix and cellulose powder.

25 The pheromone composition may be formulated as is known in the art. For example, it may be in the form of a solution, a gel, a powder. The pheromone composition may be formulated so that it can be easily dispensed, as is known in the art.

30 The present mating disruption methods may be employed in fields of transgenic crops.

Also provided herein is a method for reducing or delaying the emergence of resistance to a pesticidal trait; the method may be an integrated resistance management method. Thus are disclosed preemptive and responsive methods to delay the development of
35 resistance in a pest such as an insect, for example any of the insects listed herein, to a

transgenic insecticidal crop and/or to chemical insecticide, i.e. a preemptive strategy. Also disclosed are methods to rescue one or more pest's susceptibility to transgenic insecticidal crops and/or chemical insecticides once resistance has developed, i.e. a responsive strategy. In some embodiments, the method comprises the application of a pheromone composition, such as obtained by the methods disclosed herein, to an agricultural area comprising a field population, wherein transgenic crops comprising one or more insecticidal traits such as transgenic insecticidal traits active against one of the insects listed herein, and optionally a refuge comprising crops devoid of insecticidal traits, to disrupt mating of the pest, thereby delaying the emergence of resistance to the insecticidal trait. The present compositions may thus be used in combination with any of the methods described in WO 2017/112887.

Also provided herein is a method for preventing or reducing crop damage from a pest such as an insect as listed herein. Such methods comprise applying mating disruption to a field by applying a pheromone composition as disclosed herein, and disrupting the expression of one or more target genes in one or more pests, thereby reducing or preventing crop damage in the field. Disruption of expression of one or more target genes can be achieved using RNAi, for example as described in WO 2017/205751. The present compositions may thus be used in combination with any of the methods described in WO 2017/205751.

Examples

Example 1 – Construction of BioBricks and plasmids

All heterologous genes were synthesized by GeneArt (Life Technologies) in codon-optimized versions for *Yarrowia lipolytica*. All the genes were amplified by PCR using Phusion U Hot Start DNA Polymerase (ThermoFisher) to obtain the fragments for cloning into yeast expression vectors. The primers are listed in Table 1 and the resulting DNA fragments (BioBricks) are listed in Table 2. The PCR products were separated on a 1%-agarose gel containing Midori Green Advance (Nippon Genetics Europe GmbH). PCR products of the correct size were excised from the gel and purified using the Nucleospin Gel and PCR Clean-up kit (Macherey-Nagel).

Yeast vectors with USER cassette were linearized with FastDigest SfaAI (ThermoFisher) for 2 hours at 37°C and then nicked with Nb.BsmI (New England Biolabs) for 1 hour at 65°C. The resulting vectors containing sticky ends were

- separated by gel electrophoresis, excised from the gel, and gel-purified using the Nucleospin Gel and PCR Clean-up kit (Macherey-Nagel). The DNA fragments were cloned into vectors by USER-cloning as described in (Holkenbrink, et al., 2018). The reaction was transformed into chemically competent *E. coli* DH α cells and the cells
- 5 were plated on Lysogeny Broth (LB) agar plates with 100 mg/L ampicillin. The plates were incubated overnight at 37°C and the resulting colonies were screened by colony PCR. The plasmids were purified from overnight *E. coli* liquid cultures and the correct cloning was confirmed by sequencing. The constructed vectors are listed in Table 3.
- 10 Strains marked with “****” were constructed as follows. The indicated genes were amplified with gene-specific primers containing a 5'-overhang of “ACTTTTTCAGTACUAACCGCAG” in the forward primer and a 3'-overhang of “CACGCGAU” in the reverse primer. The first “ATG” of the target gene sequence was omitted. These PCR products were cloned together with BB9454 either into integrative
- 15 vectors or episomal vectors as described in (Holkenbrink, et al., 2018).

Table 1. Primers.

Primer ID	Template	NCBI accession number	Hybridises at positions
PR10595	Yali0C	NC_006069	1244252..1244265
PR10604	pCfB6630*		3458..3498
PR10607	Yali0A	NC_006067	483924..483945
PR11110	pCfB6681	-	2306..2336
PR11111	pCfB6681	-	5129..5152
PR14148	Yali0E	NC_006071	784691..784708
PR14279	Yali0C	NC_006069	1244254..1244265
PR15781	Yali0A	NC_006067	2188556..2188574
PR15788	Yali0A	NC_006067	456893..456922
PR15789	Yali0F	NC_006072	1948664..1948678
PR15930	Yali0C	NC_006069	1243743..1243762
PR16594	SEQ ID NO: 100	-	1..18
PR16595	SEQ ID NO: 100	-	2735..2755
PR18214	Yali0C	NC_006069	1243743..1243761

PR18928	Yali0C	NC_006069	1244252..1244265
PR20762	Yali0B	NC_006068	2566672..2566691
PR20763	Yali0B	NC_006068	2567146..2567162
PR20764	Yali0B	NC_006068	2567171..2567190
PR20765	Yali0B	NC_006068	2567645..2567662
PR21723	SEQ ID NO: 58	-	4..22
PR21724	SEQ ID NO: 58	-	997..1014
PR21806	SEQ ID NO: 70	-	4..21
PR21807	SEQ ID NO: 70	-	999..1017
PR22297	SEQ ID NO: 70	-	999..1017
PR23138	Yali0E	NC_006071	2795545..2795556
PR23139	Yali0E	NC_006071	2796053..2796036
PR23140	Yali0E	NC_006071	2795473..2795459
PR23141	Yali0E	NC_006071	2268152..2268140
PR23166	Yali0E	NC_006071	2086416..2086402
PR23167	Yali0E	NC_006071	2085907..2085919
PR23168	Yali0E	NC_006071	2086480..2086497
PR23169	Yali0E	NC_006071	2087001..2086986
PR23176	Yali0E	NC_006071	2795526..2795545
PR23177	Yali0E	NC_006071	2795526..2795545
PR23190	Yali0E	NC_006071	2086449..2086430
PR23191	Yali0E	NC_006071	2086430..2086449
PR23632	SEQ ID NO: 94	-	4..18
PR23633	SEQ ID NO: 94	-	1359..1377
PR24187	SEQ ID NO: 53	-	4..18
PR24188	SEQ ID NO: 53	-	1131..1146
PR25051	SEQ ID NO: 116	-	4..18
PR25052	SEQ ID NO: 116	-	1587..1608
PR25053	SEQ ID: 115	-	4..18
PR25054	SEQ ID: 115	-	4..18
PR25058	SEQ ID: 117	-	1545..1566
PR25075	SEQ ID NO: 118	-	4..20
PR25076	SEQ ID NO: 118	-	1998..2016
PR10852	Yali0E	NC_006071	784691..784713

PR14620	Yali0A	NC_006067	2188565..2188546
PR18241	Yali0D	NC_006070	2193232..2193213
PR18242	Yali0D	NC_006070	2193213..2193232
PR18239	Yali0C	NC_006069	568875..568856
PR18240	Yali0C	NC_006069	568856..568875
PR25309	Yali0C	NC_006069	1244237.. 1244223
PR18214	Yali0C	NC_006069	1243717.. 1243735
PR26771	SEQ ID NO: 193	-	1..20
PR26772	SEQ ID NO: 193	-	375..393
PR26773	SEQ ID NO: 194	-	4..20
PR26774	SEQ ID NO: 194	-	876..897
PR26775	SEQ ID NO: 195	-	4..25
PR26776	SEQ ID NO: 195	-	875..897
PR23004	Yali0C	NC_006069	825834.. 825853
PR13338	Yali0C	NC_006069	826765.. 826747
PR25312	Yali0C	NC_006069	1244237.. 1244223
PR25393		CP092955.1	221105.. 221090
PR25394		CP092955.1	220687.. 220703
PR25395		CP092960.1	204326.. 204346
PR25396		CP092960.1	205023.. 204999
PR26805	SEQ ID NO: 186	-	1..19
PR26806	SEQ ID NO: 186	-	2022..2040
PR26807	SEQ ID NO: 40		1..20
PR26808	SEQ ID NO: 40		936..981
PR26809	SEQ ID NO: 53		1..20
PR26810	SEQ ID NO: 53		1128..1146
PR26811	SEQ ID NO: 100		1..20
PR26812	SEQ ID NO: 100		1350..1368

*Holkenbrink et al., 2018

Table 2. DNA fragments (BioBricks) obtained by PCR using the indicated template and primers.

Bio Brick ID	Description	Template	Forward primer	Reverse primer
BB1135	Vector backbone	pCfB6681*	PR11110	PR11111
BB1631	Regions downstream of <i>Y. lipolytica pex20</i> and <i>lip2</i>	pCfB4586*	PR14148	PR15781
BB1635	Promoter for gRNA expression	pCfB4589*	PR10607	PR15788
BB1636	Terminator region for gRNA expression	pCfB4589*	PR15789	PR10604
BB1688	region upstream of <i>Y. lipolytica tef1</i>	pCfB3465*	PR14279	PR15930
BB1740	<i>Helicoverpa armigera</i> fatty acyl reductase	pCfB5390**	PR16594	PR16595
BB2093	<i>Y. lipolytica tef1</i> promoter	pCfB3516**	PR10595	PR18214
BB2311	region upstream of Fas2pI1220	ST4840**	PR20762	PR20763
BB2312	region downstream of Fas2pI1220	ST4840**	PR20764	PR20765
BB2313	Up- and downstream genomic region of Fas2p ^{I1220}	BB2311, BB2312	PR20762	PR20765
BB2693	<i>Lobesia botrana</i> desaturase	SEQ ID NO: 58	PR21723	PR21724
BB2719	region upstream of <i>Y. lipolytica tef1</i>	ST4840**	PR18928	PR18214
BB7935	<i>Spodoptera litura</i> desaturase	SEQ ID NO: 70	PR21806	PR21807
BB8250	region upstream of <i>Y. lipolytica tef1</i> and	pBP7948	PR10595	PR22297

	desaturase from <i>Spodoptera litura</i>			
BB8665	Genomic region upstream of integration site	ST4840**	PR23139	PR23138
BB8666	Genomic region downstream of integration site	ST4840**	PR23140	PR23141
BB8679	Genomic region upstream of integration site	ST4840**	PR23167	PR23166
BB8680	Genomic region downstream of integration site	ST4840**	PR23168	PR23169
BB8971	<i>Drosophila virilis</i> desaturase	SEQ ID NO: 53	PR24187	PR24188
BB9373	CDS of <i>Drosophila</i> <i>melanogaster</i> Ncb5or	SEQ ID NO: 116	PR25051	PR25052
BB9377	CDS of <i>Spodoptera litura</i> Ncb5or	SEQ ID: 118	PR25075	PR25076
BB8816	<i>Agrotis segetum</i> fatty acyl reductase	SEQ ID: 94	PR23632	PR23633
BB9374	CDS of <i>Drosophila</i> <i>grimshawi</i> Ncb5or	SEQ ID: 115	PR25053	PR25054
BB9376	CDS of <i>Homo sapiens</i> Ncb5or	SEQ ID: 117	PR25075	PR25058
BB8955	regions downstream of <i>Y.</i> <i>lipolytica pex20</i> and <i>lip2</i>	pCfB4586*	PR10852	PR14620
BB9454	<i>Y. lipolytica tef1</i> promoter	ST4840**	PR25309	PR18214
BB1010 4	<i>M. alpina</i> cytochrome B5	SEQ ID: 193	PR26771	PR26772
BB1010 5	<i>M. alpina</i> cytochrome B5 reductase 1	SEQ ID: 194	PR26773	PR26774
BB1010 6	<i>M. alpina</i> cytochrome B5 reductase 2	SEQ ID: 195	PR26775	PR26776
BB9713	<i>Y. lipolytica gpd</i> promoter	ST4840**	PR23004	PR13338

BB9457	<i>Y. lipolytica</i> <i>tef1</i> promoter	ST4840**	PR25312	PR18214
BB9510	<i>S. cerevisiae</i> <i>tef1</i> promoter	<i>S. cerevisiae</i> CEN.PK102-5B	PR25393	PR25394
BB9511	<i>S. cerevisiae</i> <i>tdh3</i> promoter	<i>S. cerevisiae</i> CEN.PK102-5B	PR25395	PR25396
BB10118	<i>C. pomonella</i> Ncb5or	SEQ ID: 186	PR26805	PR26806
BB10119	<i>A. transitella</i> desaturase	SEQ ID: 40	PR26807	PR26808
BB10120	<i>D. virilis</i> desaturase	SEQ ID: 53	PR26809	PR26810
BB10121	<i>H. armigera</i> fatty acyl-CoA reductase	SEQ ID: 100	PR26811	PR26812

* (Holkenbrink, et al., 2018)

** (Holkenbrink, et al., 2020)

Table 3. Vectors.

Plasmid ID	Resistance	Parent plasmid ID	Biobricks/primer
pBP9002	Nourseothricin	pCfB3405*	BB8955
pBP9004	Hygromycin	pCfB3431**	BB8955
pBP9556	Hygromycin	pBP9004	BB2093, BB9376
pCfB6630*	Nourseothricin		
pCfB6638*	Nourseothricin		
pBP7912	-	pCfB6684*	BB2719, BB2693
pBP7980	-	pCfB6371*	BB1688, BB1740
pBP8033	Hygromycin	pCfB3431**	BB1635, BB1636, PR18241, PR18242
pBP8138	-	pCfB6679*	BB8250
pBP8575	Nourseothricin	pCfB3405*	BB1635, BB1636, PR23190, PR23191
pBP8674	Nourseothricin	pCfB3405*	BB1635, BB1636, PR23176, PR23177

pBP8782	-	pBP8660	BB2093, BB8816
pBP9374	-	pBP8662	BB2093, BB8971
pCfB3405**	Nourseothricin		
pCfB6684*	Hygromycin		
pCfB6371*	-		
pCfB3431**	Hygromycin		
pCfB6679*	-		
pBP8660	-		BB1135, BB8665, BB1631, BB8666
pBP8662	-		BB1135, BB8679, BB8680
pCfB7088*	Nourseothricin		
pBP9546	Nourseothricin	pBP9002	BB2093, BB9373
pBP9550	Nourseothricin	pBP9002	BB2093, BB9377
pBP9553	Hygromycin	pBP9004	BB2093, BB9373
pBP9557	Hygromycin	pBP9004	BB2093, BB9377
pBP9554	Hygromycin	pBP9004	BB2093, BB9374
pBP9556	Hygromycin	pBP9004	BB2093, BB9376
pBP9547	Nourseothricin	pBP9002	BB2093, BB9374
pBP9549	Nourseothricin	pBP9002	BB2093, BB9376
pBP8032	Nourseothricin	pCfB3405	BB1635, BB1636, PR18239, PR18240
pBP8676	Hygromycin	pCfB3431	BB1635, BB1636, PR23190, PR23191
pBP10607		pBP8621	BB10104, BB10105, BB9713, BB9457
pBP10608		pBP8621	BB10104, BB10106, BB9713, BB9457
pBP10532		pBP9703***	BB9510, BB10118
pBP10533		pBP9702***	BB9511, BB10119
pBP10534		pBP9702***	BB9511, BB10120
pBP10535		pBP9702***	BB9511, BB10121

* (Holkenbrink, et al., 2018)

** (Holkenbrink, et al., 2020)

***(Jensen et al., 2014)

Example 2 – Construction of yeast strains

Yeast strains were constructed by transformation of DNA vectors as described in Holkenbrink et al., 2018 and Jensen et al., 2014. Integrative vectors were linearized with FastDigest NotI prior to transformation. When needed, helper vectors to promote the integration into specific genomic regions were co-transformed with the integrative plasmid or DNA repair fragments listed in Tables 2 and 3. Strains were selected on yeast peptone dextrose (YPD) agar with appropriate antibiotics selection. Correct genotype was confirmed by colony PCR and when needed by sequencing. Strains ST6629 is described in (Holkenbrink, et al., 2020). The resulting strains are listed in Table 4.

Table 4. Yeast strains

StrainID	Overexpressed gene	Parent strain	DNA
ST6629*	-	-	-
ST7982	-	ST6629	pCfB7088 BB2313
ST8377	FAR1 Desat35	ST7982	
ST8378	FAR1 Desat36	ST7982	
ST8373	FAR1 Desat30	ST7982	
ST8407	Desat38	ST6629	pBP8138 pCfB6638
ST8524	FAR1	ST6629	pBP7980 pCfB6630
ST9992	Desat30	ST7982	pBP7912 pBP8033
ST10609	FAR12	ST6629	pBP8782 pBP8674
ST10610	-	ST9992	pBP9002
ST10612	Desat30 DmNcb5or	ST9992	pBP9546
ST10614	Desat30 SlitNcb5or	ST9992	pBP9550
ST10615	-	ST8407	pBP9004
ST10617	Desat38 DmNcb5or	ST8407	pBP9553
ST10618	Desat38 SlitNcb5or	ST8407	pBP9557
ST10623	-	ST8524	pBP9004
ST10625	FAR1 DmNcb5or	ST8524	pBP9553
ST10626	FAR1 SlitNcb5or	ST8524	pBP9557
ST10628	Desat61	ST7982	pBP9374 pBP8575

ST10665	-	ST10609	pBP9004
ST10667	FAR12 DmNcb5or	ST10609	pBP9553
ST10668	FAR12 SlitNcb5or	ST10609	pBP9557
ST10672	-	ST10628	pBP9004
ST10674	Desat61 DmNcb5or	ST10628	pBP9553
ST10675	Desat61 SlitNcb5or	ST10628	pBP9557
ST10783	Desat38 DgNcb5or	ST8407	pBP9554
ST10785	Desat38 HsNcb5or	ST8407	pBP9556
ST10789	Desat61 DgNcb5or	ST10628	pBP9547
ST10791	Desat61 HsNcb5or	ST10628	pBP9549
ST8544	FAR1 Desat38	ST8407	pBP7980 pBP8032
ST10766	FAR1 Desat38	ST8544	pBP9002
ST10768	FAR1 Desat38 DmNcb5or	ST8544	pBP9546
ST10772	FAR1 Desat38 SlitNcb5or	ST8544	pBP9550
ST9253**	FAR1 Desat30	-	-
ST10773	FAR1 Desat30	ST9253	pBP9002
ST10775	FAR1 Desat30 DmNcb5or	ST9253	pBP9546
ST10776	FAR1 Desat30 DgNcb5or	ST9253	pBP9547
ST10778	FAR1 Desat30 HsNcb5or	ST9253	pBP9549
ST10779	FAR1 Desat30 SlitNcb5or	ST9253	pBP9550
ST8520	FAR1	ST7982	pBP7980 pBP6630
ST10629	FAR1 Desat61	ST8520	pBP9374 pBP8676
ST10661	FAR1 Desat61	ST10629	pBP9002
ST10663	FAR1 Desat61 DmNcb5or	ST10629	pBP9546
ST10780	FAR1 Desat61 DgNcb5or	ST10629	pBP9547
ST10897	CpNcb5or	ST9259	
ST10469	CpNcb5or	ST10435	
ST12511	FAR1	<i>Saccharomyces cerevisiae</i> CEN.PK102-5B	pBP9701 pBP10535 pBP9703
ST12514	FAR1 CpNcb5or	<i>Saccharomyces cerevisiae</i> CEN.PK102-5B	pBP9701 pBP10532 pBP9703

ST12510	Desat61	<i>Saccharomyces cerevisiae</i> CEN.PK102-5B	pBP9701 pBP10534 pBP9703
ST12513	Desat61 CpNcb5or	<i>Saccharomyces cerevisiae</i> CEN.PK102-5B	pBP9701 pBP10534 pBP9703
ST10624***	FAR1 CpNcb5or		
ST10786***	FAR1 DgNcb5or		
ST10787***	FAR1 LboNcb5or		
ST10788***	FAR1 HsNcb5or		
ST10666***	FAR12 CpNcb5or		
ST10616***	Desat38 CpNcb5or		
ST10784***	Desat38 LboNcb5or		
ST10611***	Desat30 CpNcb5or		
ST10613***	Desat30 LboNcb5or		
ST10673***	Desat61 CpNcb5or		
ST10790***	Desat61 LboNcb5or		
ST12195***	Desat70		
ST12178***	Desat70 CpNcb5or		
ST12003***	CpNcb5or		
ST12521***	Desat70 MaCytb5 MaCytB5Red2	ST12050	
ST12050	MaCytb5 MaCytB5Red2	ST7982	pBP10608
ST12520***	Desat70 MaCytb5 MaCytB5Red1	ST12049	
ST12049	MaCytb5 MaCytB5Red1	ST7982	pBP10607
ST12073***	FAR1 CpNcb5or		
ST12074***	FAR4 CpNcb5or		
ST12076***	FAR6 CpNcb5or		
ST12077***	FAR8 CpNcb5or		
ST12081***	FAR42 CpNcb5or		
ST12082***	FAR11 CpNcb5or		
ST12083***	FAR25 CpNcb5or		
ST12084***	FAR13 CpNcb5or		

ST12087***	FAR16 CpNcb5or		
ST12088***	FAR17 CpNcb5or		
ST12089***	FAR18 CpNcb5or		
ST12096***	FAR28 CpNcb5or		
ST12098***	FAR30 CpNcb5or		
ST12100***	FAR43 CpNcb5or		
ST12101***	FAR33 CpNcb5or		
ST12102***	FAR34 CpNcb5or		
ST12103***	FAR35 CpNcb5or		
ST12104***	FAR44 CpNcb5or		
ST12107***	FAR45 CpNcb5or		
ST12112***	FAR41 CpNcb5or		
ST12116***	FAR46 CpNcb5or		
ST12115***	FAR47 CpNcb5or		
ST12241***	Desat69 CpNcb5or		
ST12163***	Desat16 CpNcb5or		
ST12164***	Desat19 CpNcb5or		
ST12166***	Desat21 CpNcb5or		
ST12169***	Desat44 CpNcb5or		
ST12170***	Desat45 CpNcb5or		
ST12535***	Desat37 CpNcb5or		
ST12173***	Desat63 CpNcb5or		
ST12174***	Desat65 CpNcb5or		
ST12175***	Desat71 CpNcb5or		
ST12177***	Desat72 CpNcb5or		
ST12178***	Desat70 CpNcb5or		
ST12179***	Desat73 CpNcb5or		
ST12197***	Desat24 CpNcb5or		
ST12198***	Desat56 CpNcb5or		
ST12200***	Desat59 CpNcb5or		
ST12201***	Desat60 CpNcb5or		
ST12202***	Desat61 CpNcb5or		
ST12205***	Desat43 CpNcb5or		
ST12208***	Desat27 CpNcb5or		

ST12209***	Desat75 CpNcb5or		
ST12223***	Desat30 CpNcb5or		
ST12224***	Desat35 CpNcb5or		
ST12225***	Desat36 CpNcb5or		
ST12226***	Desat52 CpNcb5or		
ST12227***	Desat76 CpNcb5or		
ST12229***	Desat77 CpNcb5or		
ST12231***	Desat78 CpNcb5or		
ST12518***	AseNcb5or Desat70		
ST12007***	AseNcb5or		
ST12519***	BterNcb5or Desat70		
ST12008***	BterNcb5or		
ST12118***	FAR1		
ST12395***	AseNcb5or FAR1		
ST12397***	BterNcb5or FAR1		
ST12118***	FAR1		
ST12119***	FAR4		
ST12121***	FAR6		
ST12122***	FAR8		
ST12126***	FAR42		
ST12127***	FAR11		
ST12128***	FAR25		
ST12129***	FAR13		
ST12132***	FAR16		
ST12133***	FAR17		
ST12134***	FAR18		
ST12141***	FAR28		
ST12143***	FAR30		
ST12145***	FAR43		
ST12146***	FAR33		
ST12147***	FAR34		
ST12148***	FAR35		
ST12149***	FAR44		
ST12152***	FAR45		

ST12157***	FAR41		
ST12161***	FAR46		
ST12160***	FAR47		
ST12242***	Desat69		
ST12180***	Desat16		
ST12181***	Desat19		
ST12183***	Desat21		
ST12186***	Desat44		
ST12187***	Desat45		
ST12534***	Desat37		
ST12190***	Desat63		
ST12191***	Desat65		
ST12192***	Desat71		
ST12194***	Desat72		
ST12195***	Desat70		
ST12196***	Desat73		
ST12210***	Desat24		
ST12211***	Desat56		
ST12213***	Desat59		
ST12214***	Desat60		
ST12215***	Desat61		
ST12218***	Desat43		
ST12221***	Desat27		
ST12222***	Desat75		
ST12232***	Desat30		
ST12233***	Desat35		
ST12234***	Desat36		
ST12235***	Desat52		
ST12236***	Desat76		
ST12238***	Desat77		
ST12240***	Desat78		

* (Holkenbrink, et al., 2020)

** (Petkevicius, et al., 2021)

*** For description of strain constructions see text

Example 3 – Cultivation of strains and analysis of fatty alcohols and fatty acid methyl esters (FAME)

Strains were inoculated from a YPD agar plate (10 g/L yeast extract, 10 g/L peptone, 20 g/L glucose, 15 g/L agar agar) to an initial OD600 of 0.1-0.2 into 2.5 mL YPG medium (10 g/L yeast extract, 10 g/L peptone, 40 g/L glycerol) in 24 well-plates (EnzyScreen). The plates were incubated at 28°C, shaken at 300 rpm. After 24 h, the plates were centrifuged for 5 min at 3,000 xg. The supernatant was discarded and the cells were resuspended in 1.25 mL production medium per well (50 g/L glycerol, 5 g/L yeast extract, 4 g/L KH₂PO₄, 1.5 g/L MgSO₄, 0.2 g/L NaCl, 0.265 g/L CaCl₂·2H₂O, 2 mL/L trace elements solution: 4.5 g/L CaCl₂·2H₂O, 4.5 g/L ZnSO₄·7H₂O, 3 g/L FeSO₄·7H₂O, 1 g/L H₃BO₃, 1 g/L MnCl₂·4H₂O, 0.4 g/L N Na₂MoO₄·2H₂O, 0.3 g/L CoCl₂·6H₂O, 0.1 g/L CuSO₄·5H₂O, 0.1 g/L KI, 15 g/L EDTA). The media was supplemented with antibiotics if necessary. The plate was incubated for 26 hours at 28°C, shaken at 300 rpm.

For analysis of fatty alcohols, 1 mL of fermentation broth was harvested from each vial and biomass was separated by centrifugation for 5 min at 3,000 xg. Biomass pellets were extracted with 990 µL of ethyl acetate:ethanol (84:15) and 10 µL of 19:Me (2 mg/mL) as internal standard. The samples were vortexed for 20 sec and incubated for 1 h at room temperature, followed by 5 min of vortexing. 300 µL of H₂O was added to each sample. The samples were vortexed and centrifuged for 5 min at 21°C and 3,000 x g. The upper organic phase was analyzed via gas chromatography-mass spectrometry (GC-MS). GC-MS analyses were performed on an Agilent 7820A GC coupled to a mass selective detector Agilent 5977B. The GC was equipped with a DB Fatwax column (30 m×0.25mm ×0.25 µm), and helium was used as carrier gas. The MS was operated in electron impact mode (70eV), scanning between m/z 30 and 400, and the injector was configured in split mode 20:1 at 220°C. Oven temperature was set to 80°C for 1 min, then increased at a rate of 20°C /min to 210°C, followed by a hold at 210°C for 7 min, and then increased at a rate of 20 C/min to 230°C. Compounds were identified by comparison of retention times and mass spectra of the reference compounds. Compounds were quantified by the ion 55.1 m/z. Data were analyzed by the Agilent Masshunter software. The concentrations of fatty alcohols were calculated based on standard calibration curves prepared with reference standards.

For analysis of FAMES, 1 mL of fermentation broth was harvested from each vial and biomass was separated by centrifugation for 5 min at 3,000 xg. Biomass pellets were extracted with 1000 µL 1M HCl in Methanol (anhydrous). The samples were vortexed for 20 sec and placed in the 80°C water bath for 2 h. The samples were vortexed every 30 min for 10 sec. After cooling down of the samples to room temperature, 1000 µL of 1M NaOH in Methanol (anhydrous), 500 µL of NaCl saturated H₂O, 990 µL of hexane and 10 µL of 19:Me (2 mg/mL) as internal standard were added. The samples were vortexed and centrifuged for 5 min at 21°C and 3,000 xg. The upper organic phase was analyzed via GC-MS as described above.

Example 4 – Putative Ncb5or-coding genes from insects

Putative Ncb5or proteins from Lepidoptera can be seen in Table 5. Each protein contains a cytochrome b5, a cytochrome b5 reductase, and an SGD1-CHORD domain.

Table 5. Non-exhaustive list of Lepidoptera Ncb5ors.

Description	Species	Accession
cytochrome b5 reductase 4 isoform X1	<i>Manduca sexta</i>	XP_030040351.1
PREDICTED: cytochrome b5 reductase 4 isoform X1	<i>Amyelois transitella</i>	XP_013199405.1
cytochrome b5 reductase 4 isoform X1	<i>Spodoptera litura</i>	XP_022822658.1
hypothetical protein evm_009546	<i>Chilo suppressalis</i>	RVE45796.1
cytochrome b5 reductase 4 isoform X1	<i>Galleria mellonella</i>	XP_026756471.1
cytochrome b5 reductase 4	<i>Bombyx mori</i>	XP_012550604.1
cytochrome b5 reductase 4 isoform X1	<i>Bombyx mandarina</i>	XP_028042050.1
cytochrome b5 reductase 4 isoform X1	<i>Helicoverpa armigera</i>	XP_021195006.1
cytochrome b5 reductase 4 isoform X1	<i>Danaus plexippus</i> <i>plexippus</i>	XP_032518662.1
cytochrome b5 reductase 4 isoform X1	<i>Bicyclus anynana</i>	XP_023948592.1
cytochrome b5 reductase 4 isoform X1	<i>Vanessa tameamea</i>	XP_026495955.1
PREDICTED: cytochrome b5 reductase 4-like	<i>Papilio polytes</i>	XP_013148264.1
PREDICTED: cytochrome b5 reductase 4-like isoform X1	<i>Papilio xuthus</i>	XP_013179866.1

PREDICTED: cytochrome b5 reductase 4-like isoform X2	<i>Papilio xuthus</i>	XP_013179867.1
PREDICTED: cytochrome b5 reductase 4-like	<i>Papilio machaon</i>	XP_014360030.1
cytochrome b5 reductase 4-like isoform X1	<i>Pieris rapae</i>	XP_022127972.1
cytochrome b5 reductase 4 isoform X1	<i>Hypsmocoma kahamanoa</i>	XP_026321155.1
cytochrome b5 reductase 4 isoform X2	<i>Bicyclus anynana</i>	XP_023948593.1
cytochrome b5 reductase 4 isoform X2	<i>Spodoptera litura</i>	XP_022822662.1
PREDICTED: cytochrome b5 reductase 4 isoform X3	<i>Amyelois transitella</i>	XP_013199409.1
PREDICTED: cytochrome b5 reductase 4-like isoform X1	<i>Papilio polytes</i>	XP_013148114.1
cytochrome b5 reductase 4 isoform X3	<i>Manduca sexta</i>	XP_030040353.1
cytochrome b5 reductase 4 isoform X3	<i>Spodoptera litura</i>	XP_022822663.1
cytochrome b5 reductase 4 isoform X3	<i>Helicoverpa armigera</i>	XP_021195008.1
hypothetical protein B5X24_HaOG207824	<i>Helicoverpa armigera</i>	PZC74467.1
cytochrome b5 reductase 4 isoform X2	<i>Helicoverpa armigera</i>	XP_021195007.1
PREDICTED: cytochrome b5 reductase 4 isoform X2	<i>Amyelois transitella</i>	XP_013199408.1
cytochrome b5 reductase 4 isoform X2	<i>Hypsmocoma kahamanoa</i>	XP_026321156.1
cytochrome b5 reductase 4 isoform X3	<i>Galleria mellonella</i>	XP_026756473.1
cytochrome b5 reductase 4 isoform X2	<i>Bombyx mandarina</i>	XP_028042054.1
cytochrome b5 reductase 4 isoform X2	<i>Galleria mellonella</i>	XP_026756472.1
cytochrome b5 reductase 4 isoform X2	<i>Vanessa tameamea</i>	XP_026495958.1
cytochrome b5 reductase 4 isoform X3	<i>Vanessa tameamea</i>	XP_026495959.1
Cytochrome b5 reductase 4	<i>Papilio xuthus</i>	KPI97000.1
PREDICTED: cytochrome b5 reductase 4-like isoform X3	<i>Papilio xuthus</i>	XP_013179870.1
cytochrome b5 reductase 4 isoform X3	<i>Danaus plexippus plexippus</i>	XP_032518665.1

cytochrome b5 reductase 4 isoform X2	<i>Danaus plexippus plexippus</i>	XP_032518664.1
cytochrome b5 reductase 4 isoform X4	<i>Danaus plexippus plexippus</i>	XP_032518666.1
cytochrome b5 reductase 4-like isoform X2	<i>Pieris rapae</i>	XP_022127974.1
cytochrome b5 reductase 4-like isoform X3	<i>Pieris rapae</i>	XP_022127975.1
PREDICTED: cytochrome b5 reductase 4-like	<i>Papilio machaon</i>	XP_014360076.1
PREDICTED: cytochrome b5 reductase 4-like isoform X2	<i>Papilio xuthus</i>	XP_013179773.1
PREDICTED: cytochrome b5 reductase 4-like isoform X1	<i>Papilio xuthus</i>	XP_013179772.1
hypothetical protein KGM_216032	<i>Danaus plexippus plexippus</i>	OWR44507.1
Cytochrome b5 reductase 4	<i>Papilio machaon</i>	KPJ13840.1
cytochrome b5 reductase 4-like	<i>Pieris rapae</i>	XP_022122274.1
Cytochrome b5 reductase 4	<i>Papilio xuthus</i>	KPI97001.1

Example 5 – Ncb5or co-expression increases the activity of fatty acyl-CoA reductases

Two insect Ncb5or genes were co-expressed in *Y. lipolytica* in combination with a fatty acyl-CoA reductase from *Helicoverpa armigera* (FAR1) or a fatty acyl-CoA reductase from *Agrotis segetum* (FAR12), respectively. The strains were cultivated, and fatty alcohols analyzed as described in Example 3.

The presence of insect Ncb5or improved the activity of FAR1 reductase in *Y. lipolytica* by 15-25% (Table 6) and of FAR12 by 16% (Table 7).

Table 6. Effect of Ncb5or on the activity of reductase FAR1 from *H. armigera*.

Strain	Ncb5or	Total fatty alcohols (mg/L)	Improvement (%)
ST10623	-	361 ± 34	Reference
ST10625	DmNcb5or	415 ± 38	15
ST10626	SlitNcb5or	451 ± 10	25

Table 7. Effect of Ncb5or on the activity of reductase FAR12 from *A. segetum*.

Strain	Ncb5or	Total fatty alcohols (mg/L)	Improvement (%)
ST10665	-	80 ± 18	Reference
ST10667	DmNcb5or	93 ± 32	16
ST10668	SlitNcb5or	62 ± 7	NA

Example 6 – Ncb5or co-expression increases the activity of fatty acyl-CoA desaturases

Three insect and one human Ncb5or genes were co-expressed in *Y. lipolytica* in combination with a fatty acyl-CoA desaturase from *Spodoptera litura* (Desat38), or a fatty acyl-CoA desaturase from *Lobesia botrana* (Desat30), or a fatty acyl-CoA desaturase from *Drosophila virilis* (Desat61), respectively. The strains were cultivated and FAMES analyzed as described in Example 3.

The presence of insect Ncb5or improved the activity of Desat38 desaturase in *Y. lipolytica* by 13 to 42% (Table 8), Desat30 by 9-36% (Table 9), and Desat61 by 3-34% (Table 10).

Table 8. Effect of Ncb5or on the activity of desaturase Desat38 from *S. litura*.

Strain	Ncb5or	Z11-16:Me purity (%)	Improvement (%)
ST10615	-	26 ± 0	Reference
ST10617	DmNcb5or	36 ± 2	38
ST10618	SlitNcb5or	36 ± 2	42
ST10783	DgNcb5or	32 ± 3	24
ST10785	HsNcb5or	29 ± 2	13

Table 9. Effect of Ncb5or on the activity of desaturase Desat30 from *L. botrana*. Strains in this table carry a mutation in Fas2p that increases tetradecanoyl-CoA biosynthesis.

Strain	Ncb5or	Z11-14:Me (mg/L)	Improvement (%)
ST10610	-	11 ± 2	Reference
ST10612	DmNcb5or	15 ± 0	36
ST10614	SlitNcb5or	12 ± 1	9

Table 10. Effect of Ncb5or on the activity of desaturase Desat61 from *D. virilis*. Strains in this table carry a mutation in Fas2p that increases tetradecanoyl-CoA biosynthesis.

Strain	Ncb5or	Z9-14:Me purity (%)	Improvement (%)
ST10672	-	3 ± 0	Reference
ST10674	DmNcb5or	4 ± 1	9
ST10675	SlitNcb5or	4 ± 0	12
ST10789	DgNcb5or	3 ± 0	3
ST10791	HsNcb5or	5 ± 0	34

Example 7 – Ncb5or co-expression increases the production of Z11-16:OH in Y.

lipolytica

Two insect Ncb5or genes were co-expressed in *Y. lipolytica* previously engineered for production of Z11-16:OH. The strains were cultivated and fatty alcohols analyzed as described in Example 3.

The presence of insect Ncb5or improved the titer of Z11-16:OH by 69-82% (Table 11). Furthermore, both Ncb5or proteins, DmNcb5or and SlitNcb5or, increased the purity of Z11-16:OH (Table 11).

Table 11. Effect of Ncb5or on the production of Z11-16:OH.

Strains	Ncb5or	Z11-16:OH (mg/L)	Improvement of Z11-16:OH (%)	Total fatty alcohols (mg/L)	Z11-16:OH purity (%)
ST10766	-	87 ± 9	Reference	184 ± 15	47 ± 2
ST10768	DmNcb5or	159 ± 2	82	241 ± 9	66 ± 2
ST10772	SlitNcb5or	260 ± 8	69	378 ± 5	69 ± 2

Example 8 – Ncb5or co-expression increases the production of Z11-14:OH in Y.

lipolytica

Three insect Ncb5or and one human Ncb5or genes were co-expressed in *Y. lipolytica* previously engineered for production of Z11-14:OH. The strains were cultivated and fatty alcohols analyzed as described in Example 3.

The presence of insect Ncb5or improved the titer of Z11-14:OH by 8-13% (Table 12). Furthermore, several Ncb5or proteins (DmNcb5or, DgNcb5or) increased the purity of Z11-14:OH (Table 12).

5 **Table 12.** Effect of Ncb5or on the production of Z11-14:OH.

Strains	Ncb5or	Z11-14:OH (mg/L)	Improvement of Z11-14:OH (%)	Total fatty alcohol (mg/L)	Z11-14:OH purity (%)
ST10773	-	161 ± 19	Reference	1053 ± 112	15 ± 1
ST10775	DmNcb5or	174 ± 16	8	837 ± 77	21 ± 0
ST10776	DgNcb5or	181 ± 15	13	1026 ± 110	18 ± 0
ST10778	HsNcb5or	122 ± 78	NA	706 ± 415	20 ± 8
ST10779	SlitNcb5or	154 ± 13	NA	711 ± 55	27 ± 2

Example 9 – Ncb5or co-expression increases the production of Z9-14:OH in Y. lipolytica

- 10 Two insect Ncb5or genes were co-expressed in *Y. lipolytica* previously engineered for production of Z9-14:OH. The strains were cultivated and fatty alcohols analyzed as described in Example 3.

The presence of insect Ncb5or improved the titer of Z9-14:OH by 25-46% (Table 13).

- 15 Furthermore, the DmNcb5or proteins increased the purity of Z9-14:OH (Table 13).

Table 13. Effect of Ncb5or on the production of Z9-14:OH.

Strains	Ncb5or	Z9-14:OH (mg/L)	Improvement of Z9-14:OH (%)	Total fatty alcohol (mg/L)	Z9-14:OH purity (%)
ST10661	-	75 ± 13	Reference	251 ± 43	30 ± 1
ST10663	DmNcb5or	93 ± 3	25	278 ± 10	34 ± 0

ST10780	DgNcb5or	109 ± 23	46	347 ± 59	31 ± 1
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Example 10 – Ncb5or expression in strain engineered for high production of Z11-16:OH and Z9-14:OH

5 The Ncb5or from *Cydia pomonella*, CpNcb5or, was expressed in *Y. lipolytica* strains ST9259 and ST10435 engineered to produce high titers of Z11-16:OH and Z9-14:OH, respectively, resulting in strain ST10897 and ST10469, respectively. The strains were cultivated and fatty alcohols analyzed as described in Example 3. Strain ST10897 and ST10469 produced 44% more of Z11-16:OH and 75% more of Z9-14:OH than the
10 control strains ST9259 and ST10435, respectively.

Example 11 – Co-expression of multiple Ncb5or in one production strain

Two Ncb5or are expressed in strain ST8544 and/or in a *Y. lipolytica* strain producing high titers of Z11-16:OH or Z9-14:OH. The strains are cultivated and fatty alcohols
15 analyzed as described in Example 3.

Example 12 – Ncb5or expression in the yeast S. cerevisiae

An insect Ncb5or was co-expressed in the yeast *S. cerevisiae* together with either the Desat61 desaturase, or the fatty acyl reductase FAR1. The strains were inoculated in
20 2.5 ml yeast synthetic drop-out medium (1.39 g/L yeast synthetic drop-out medium without histidine, leucine, tryptophan and uracil (Sigma Aldrich, Y2001), 6.7 g/L yeast nitrogen base without amino acids (Sigma Aldrich Y0626), 20 g/L glucose) to an OD600 of 0.2. The strains were cultivated in 24-well deep-well plates (EnzyScreen) in triplicates and incubated for 24 hours at 28 h with shaking at 250 rpm. After 24 hours
25 the cells were pelleted by centrifugation, the supernatant discarded and replaced by 1.5 ml fresh yeast synthetic drop-out medium. The fatty alcohols/FAMEs were analyzed as described in Example 3. Strain ST12511 expressing fatty acyl reductase FAR1 produced 3.2 ± 0.1 mg/L total fatty alcohols while strain ST12514 co-expressing the Ncb5or of *Cydia pomonella* with FAR1 produced 3.9 ± 0.7 mg/L total fatty alcohols,
30 corresponding to an 22% improvement. In strain ST12510, expressing ΔZ9-14 desaturase Desat61 from *Drosophila virilis*, Z9-14:Me accounts for 9.3 ± 0.2% of the total fatty acids, while in strain ST12513 co-expressing the Ncb5or of *Cydia pomonella* and Desat61 Z9-14:Me accounted for 9.4±0.3% of the total fatty acids.

Example 13 – Co-expression of Lepidoptera desaturase and Ncb5or in plants

Wild-type *Nicotiana benthamiana* plants are grown in a greenhouse or growth chamber. An insect Ncb5or and desaturase are cloned into a plant expression vector and electroporated into *Agrobacterium tumefaciens*. The transformed strain was cultivated in LB medium and the expression of virulence genes was induced by addition of acetosyringone to the medium. The culture was diluted in infiltration buffer and applied to the underside of *N. benthamiana* leaf and slight pressure applied to the leaf. Plants were grown for four more days. For lipid analysis, ~100 mg of fresh leaf is used. The lipid extraction was as for yeast cells described in Example 3.

Instead of *Nicotiana benthamiana* plants and oleogenous plant could be chosen as a host. The plants are cultivated. The desired desaturated fatty acids accumulate in plant lipids. The fatty acids can be recovered from plant lipids by methods known in the art, e.g. after homogenisation of the plants and recovery of the lipids by methods known in the art. The recovered lipids are hydrolyzed into free fatty acids and esterified to fatty acid alkyl ester, followed by a reduction to either fatty alcohols or fatty aldehydes.

Example 14 – Desaturase specificity

The activities and specificities of desaturases were tested in a *S. cerevisiae* strain with deletions of *OLE1* and *ELO1* genes, encoding for Δ^9 -fatty acid desaturase and medium-chain acyl elongase respectively. Three individual colonies of strains ST_Desat18, ST_Desat17, ST_Desat22, ST_Desat23, ST_ScOLE1 and ST_DmeD9 were inoculated into 1 mL selective media (SC-Ura-Leu) and incubated at 30°C and 300 rpm for 48 h. The cultures were diluted to an OD600 of 0.4 in 5 mL selective medium supplemented with 2 mM CuSO₄ and the 0.5 mM methyl myristate (14:Me) (Larodan Fine Chemicals, Sweden). The methyl myristate stock solution was prepared to a concentration of 100 mM in 96% ethanol. The yeast cultures were incubated at 30°C at 300 rpm for 48 hours.

1 mL of culture was sampled and 3.12 µg of nonadecylic acid methyl ester was added as internal standard. Total lipids were extracted using 3.75 mL of methanol/chloroform (2:1, v/v), in a glass vial. One mL of acetic acid (0.15 M) and 1.25 mL of water were added to the tube. Tubes were vortexed vigorously and centrifuged at 2,000xg for 2 min. The bottom chloroform phase, about 1 mL, containing the total lipids, was transferred to a new glass vial and the solvent was evaporated to dryness. Fatty acid

methyl esters (FAMES) were made from this total lipid extract by acid methanolysis. One mL of 2% sulfuric acid in methanol (v/v) was added to the tube, vortexed vigorously, and incubated at 90°C for 1 h. After incubation, 1 mL of water was added and mixed well, and then 1 mL of hexane was used to extract the FAMES.

5

The methyl ester samples were subjected to GC-MS analyses on a Hewlett Packard 6890 GC coupled to a mass selective detector HP 5973. The GC was equipped with an INNOWax column (30 m×0.25 mm×0.25 µm), and helium was used as the carrier gas (average velocity: 33 cm/s). The MS was operated in electron impact mode (70 eV), and the injector was configured in splitless mode at 220°C. The oven temperature was set to 80°C for 1 min, then increased at a rate of 10°C/min up to 210°C, followed by a hold at 210°C for 15 min, and then increased at a rate of 10°C/min up to 230°C followed by a hold at 230°C for 20 min. The monounsaturated fatty-acid products were identified by comparing their retention times and mass spectra with those of synthetic standards. Data were analyzed by the ChemStation software (Agilent Technologies, USA).

10

15

The measured concentrations of Z9-14:Me and Z9-16:Me (Table 14) show that strain ST_DmeD9, expressing desaturase from *D. melanogaster*, resulted in the highest concentration of Z9-14:Me (3.67 mg/L) and in the maximal ratio of Z9-14:Me and Z9-16:Me. This indicates that among the tested desaturases, *D. melanogaster* desaturase has the highest activity and specificity towards C14-CoA substrate.

20

Table 14. Activity and specificity of heterologous desaturases in yeast.

Strain name	Over-expressed desaturase	Parent strain (key characteristics)	Vectors introduced into parent strain	Z9-14:Me (mg/L)	Z9-16:Me (mg/L)	Ratio of 14:1/16:1 [specificity]
ST_Desat18	Desat18	$\Delta ole1\Delta elo1$	pYEX-CHT-Desat18	0.25	0.56	0.45
ST_Desat17	Desat17	$\Delta ole1\Delta elo1$	pYEX-CHT-Desat17	0.03	0.13	0.20
ST_Desat22	Desat22	$\Delta ole1\Delta elo1$	pYEX-CHT-Desat22	0.00	0.00	0.00

ST_Desat23	Desat23	$\Delta ole1\Delta elo1$	pYEX-CHT-Desat23	0.00	0.00	0.00
ST_ScOLE1	ScOLE1	$\Delta ole1\Delta elo1$	pYEX-CHT-OLE1	0.39	3.01	0.13
ST_DmeD9	Desat24	$\Delta ole1\Delta elo1$	pYEX-CHT-Desat24	3.67	0.24	15.29

Strains ST8377, ST8378 and ST8373 were also tested for production of desaturated C14 compounds. Fatty alcohols were extracted from these strains after cultivation and analysed by GC-MS. Titers are shown in Table 15.

5

Table 15. Titers obtained in strains expressing FAR1 and a desaturase as indicated. Titers are in mg/L. The shaded columns indicate the titers of the desaturated fatty alcohols E11-14:OH, Z11-14:OH, Z9-16:OH and Z11-16:OH.

Strain ID	Desaturase introduced	14:OH	Z9-14:OH	E11-14:OH	Z11-14:OH	16:OH	Z9-16:OH	Z11-16:OH
ST8225 (control)	none	214.75 ± 36.86	1.26 ± 0.21	0.00 ± 0.00	0.00 ± 0.00	76.98 ± 14.71	26.56 ± 2.12	1.31 ± 0.88
ST8377	Desat35	169.57 ± 8.58	2.31 ± 0.18	0.90 ± 0.10	2.09 ± 0.03	57.13 ± 1.63	20.62 ± 0.22	2.51 ± 0.10
ST8378	Desat36	193.04 ± 12.42	3.29 ± 0.09	0.30 ± 0.13	0.00 ± 0.00	59.42 ± 1.10	24.45 ± 1.24	2.68 ± 0.19
ST8373	Desat30	296.40 ± 17.20	2.29 ± 0.07	1.46 ± 0.22	21.53 ± 2.16	107.77 ± 8.03	37.91 ± 1.99	3.09 ± 0.62

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As can be seen, the control strain expressing the FAR1 reductase but no desaturase was able to produce the C16 fatty alcohols Z9-16:OH and Z11-16:OH, but did not produce any detectable C14 fatty alcohols (E11-14:OH and Z11-14:OH). The three tested strains were also able to produce the C16 fatty alcohols, and all of them were in addition able to produce the C14 fatty alcohols Z11-14:OH, and to a lesser degree also E11-14:OH. The above data also show that none of the three tested desaturases,

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when introduced in the cell, results in significant changes in production of Z11-16:OH compared to the control strain without desaturase. The data thus show that these three desaturases also have a higher specificity towards C14 substrates than towards C16 substrates.

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Example 15 – Co-expression of fatty acyl-CoA reductases with Ncb5or

Three insect Ncb5or and one human Ncb5or gene were co-expressed in *Y. lipolytica* in combination with a fatty acyl-CoA reductase from *Helicoverpa armigera* (FAR1) or one insect Ncb5or was co-expressed with a fatty acyl-CoA reductase from *Agrotis segetum* (FAR12). The strains were cultivated, and fatty alcohols analyzed as described in Example 3.

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The presence of insect Ncb5or improved the activity of FAR1 reductase in *Y. lipolytica* by 3-10% (Table 16) and of FAR12 by 4% (Table 17).

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Table 16. Effect of Ncb5or on the activity of reductase FAR1 from *H. armigera*.

Strain	Ncb5or	Total fatty alcohols (mg/L)	Improvement (%)
ST10623	-	819 ± 84	Reference
ST10624	CpNcb5or	900 ± 23	10
ST10786	DgNcb5or	890 ± 250	9
ST10787	LboNcb5or	841 ± 21	3
ST10788	HsNcb5or	687 ± 50	-16

Table 17. Effect of Ncb5or on the activity of reductase FAR12 from *A. segetum*.

Strain	Ncb5or	Total fatty alcohols (mg/L)	Improvement (%)
ST10665	-	80 ± 18	Reference
ST10666	CpNcb5or	83 ± 15	4

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Example 16 – Co-expression of fatty acyl-CoA desaturases with Ncb5or

Two insect Ncb5or genes were co-expressed in *Y. lipolytica* in combination with a fatty acyl-CoA desaturase from *Spodoptera litura* (Desat38), or a fatty acyl-CoA desaturase from *Lobesia botrana* (Desat30), or a fatty acyl-CoA desaturase from *Drosophila virilis* (Desat61), respectively. The strains were cultivated and FAMES analyzed as described in Example 3.

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The presence of insect Ncb5or improved the activity of Desat38 desaturase in *Y. lipolytica* by 26 to 36% (Table 18), Desat30 by 9-27% (Table 19), and Desat61 by 11-21% (Table 20).

5 **Table 18.** Effect of Ncb5or on the activity of desaturase Desat38 from *S. litura*.

Strain	Ncb5or	Z11-16:Me purity (%)	Improvement (%)
ST10615	-	26 ± 0	Reference
ST10616	CpNcb5or	36	38
ST10784	LboNcb5or	33	26

Table 19. Effect of Ncb5or on the activity of desaturase Desat30 from *L. botrana*.

Strains in this table carry a mutation in Fas2p that increases tetradecanoyl-CoA biosynthesis.

Strain	Ncb5or	Z11-14:Me (mg/L)	Improvement (%)
ST10610	-	11 ± 2	Reference
ST10611	CpNcb5or	14 ± 0	27
ST10613	LboNcb5or	12 ± 3	9

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Table 20. Effect of Ncb5or on the activity of desaturase Desat61 from *D. virilis*. Strains in this table carry a mutation in Fas2p that increases tetradecanoyl-CoA biosynthesis.

Strain	Ncb5or	Z9-14:Me purity (%)	Improvement (%)
ST10672	-	3 ± 0	Reference
ST10673	CpNcb5or	4 ± 0	21
ST10790	LboNcb5or	4 ± 0	11

15 **Example 17– Cytochrome B5 and cytochrome B5 reductase from *Mortierella alpina* co-expression with desaturase**

A cytochrome B5 (MaCytB5) and cytochrome B5 reductase 1 or 2 (MaCytB5 Red1 or 2), respectively, of *Mortierella alpina* or Ncb5or from *Cydia pomonella* (CpNcb5or) were co-expressed in *Y. lipolytica* in combination with fatty acyl-CoA Δ 11 desaturase from

20 *Cadra cautella* (Desat70). The resulting strains are listed in Table 21.

Combining the expression of Desat70 with the *C.pomonella* Ncb5or improved the purity of Z11-16:Me by 46% compared to a strain expressing only Desat70, while when

combined with the cytochrome B5 and cytochrome B5 reductase pairs from *M. alpina* the purity improved only 14 and 29%.

Table 21. Effect of Ncb5or from *C. pomonella* or cytochrome B5 and B5 reductase from *M. alpina* on the activity of fatty acyl-CoA desaturase Desat70. Strains in this table carry a mutation in Fas2p that increases tetradecanoyl-CoA biosynthesis.

Strain	Genes expressed	Z11-16:Me purity (%)	Improvement (%)
ST12195	Desat70	13.8 ± 1	-
ST12178	Desat70 CpNcb5or	20.2 ± 0.1	46
ST12521	Desat70 MaCytb5 MaCytB5Red2	15.7 ± 2	14
ST12520	Desat70 MaCytb5 MaCytB5Red1	17.8 ± 3	29

Example 18 – Ncb5or from Cydia pomonella co-expression with various fatty acyl Co-A reductase

Fatty acyl-CoA reductases from different organisms were either expressed alone (control strains) or in combination with Ncb5or of *Cydia pomonella* (CpNcb5or). The strains were cultivated, and fatty alcohols analyzed as described in Example 3, except from that the cells were inoculated into YPG medium without adjustment of the optical density and the incubation in YPG medium was prolonged from 24 to 48 hours. The total fatty alcohol production titers of the strains are shown in Table 22. Total fatty alcohol production improvements between 0-50% in comparison to the control are marked with a "+", 51-100% with a "++" and >100% with a "+++".

The expression of Ncb5or from *Cydia pomonella* improved the activity all fatty acyl Co-A reductases in *Y. lipolytica* (Table 22).

Table 22. Effect of Ncb5or from *Cydia pomonella* on production of fatty alcohols by indicated fatty acyl-CoA reductases

Strain expressing CpNcb5or	Fatty acyl-CoA reductase	Control strain without CpNcb5or	Improvement in total fatty alcohol production over control
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ST12073	FAR2	ST12118	+
ST12074	FAR4	ST12119	+
ST12076	FAR6	ST12121	+
ST12077	FAR8	ST12122	++
ST12081	FAR42	ST12126	+++
ST12082	FAR11	ST12127	+
ST12083	FAR25	ST12128	+
ST12084	FAR13	ST12129	++
ST12087	FAR16	ST12132	+++
ST12088	FAR17	ST12133	+++
ST12089	FAR18	ST12134	+
ST12096	FAR28	ST12141	++
ST12098	FAR30	ST12143	+
ST12100	FAR43	ST12145	+
ST12101	FAR33	ST12146	++
ST12102	FAR34	ST12147	+++
ST12103	FAR35	ST12148	++
ST12104	FAR44	ST12149	+
ST12107	FAR45	ST12152	+
ST12112	FAR41	ST12157	+
ST12116	FAR46	ST12161	++
ST12115	FAR47	ST12160	+

Example 19 – Ncb5or from Cydia pomonella co-expression with various fatty acyl Co-A desaturases

Fatty acyl-CoA desaturases from different organisms were either expressed alone
 5 (control strains) or in combination with Ncb5or of *Cydia pomonella* (CpNcb5or). The strains were cultivated, and FAME analysis were performed as described in Example 3, except from that the cells were inoculated into YPG medium without adjustment of optimal density and the incubation time in YPG medium was prolonged from 24 to 48 hours. The purity of the target desaturated fatty acid methyl esters are shown in Table
 10 23. Purity improvements between 0-50% in comparison to the control are marked with a "+", 51-100% with a "++" and >100% with a "+++".

All desaturases listed below showed a higher activity when combined with Ncb5or from *Cydia pomonella*.

15 **Table 23.** Effect of Ncb5or from *Cydia pomonella* on production of desaturated fatty acid methyl esters by indicated fatty acyl-CoA desaturases

Strain expressing CpNcb5or	Fatty acyl-CoA desaturase	Target fatty acid methyl ester	Control strain without CpNcb5or	Improvement in purity (%)
ST12241	Desat69	Z9-14:Me	ST12242	+
ST12241	Desat69	Z9-16:Me	ST12242	+
ST12241	Desat69	Z9-18:Me	ST12242	+
ST12163	Desat16	Z11-16:Me	ST12180	+
ST12164	Desat19	Z11-16:Me	ST12181	+
ST12166	Desat21	Z11-16:Me	ST12183	+
ST12169	Desat44	Z11-16:Me	ST12186	+
ST12170	Desat45	Z11-16:Me	ST12187	+
ST12535	Desat37	Z11-16:Me	ST12534	+
ST12173	Desat63	Z11-16:Me	ST12190	+++
ST12174	Desat65	Z11-16:Me	ST12191	+
ST12175	Desat71	Z11-16:Me and Z11-18:Me	ST12192	++
ST12177	Desat72	Z11-16:Me and Z11-18:Me	ST12194	+
ST12178	Desat70	Z11-16:Me	ST12195	+
ST12179	Desat73	Z11-16:Me	ST12196	+++
ST12197	Desat24	Z9-14:Me	ST12210	++
ST12198	Desat56	Z9-14:Me	ST12211	++
ST12200	Desat59	Z9-14:Me	ST12213	++
ST12201	Desat60	Z9-14:Me	ST12214	++
ST12202	Desat61	Z9-14:Me	ST12215	++
ST12205	Desat43	Z9-16:Me	ST12218	+
ST12208	Desat27	Z9-14:Me and Z9-16:Me	ST12221	+
ST12209	Desat75	Z9-14:Me and Z9-16:Me	ST12222	+++
ST12223	Desat30	E11-14:Me and Z11-14:Me	ST12232	+++
ST12224	Desat35	E11-14:Me and Z11-14:Me	ST12233	+++
ST12225	Desat36	E11-14:Me and Z11-14:Me	ST12234	+++
ST12226	Desat52	E11-14:Me and Z11-14:Me	ST12235	+++
ST12227	Desat76	E11-14:Me and Z11-14:Me	ST12236	+++
ST12229	Desat77	E14-16:Me	ST12238	+
ST12231	Desat78	Z11-18:Me	ST12240	+

Example 20 – Co-expression of Ncb5or from Agrotis segetum or Bombus terrestris with desaturase Desat70 or fatty acyl Co-A reductase

Ncb5or genes from *Agrotis segetum* and *Bombus terrestris* were co-expressed in *Y. lipolytica* in combination with the *Cadra cautella* desaturase Desat70 or a fatty acyl-CoA reductase from *Helicoverpa armigera* (FAR1), respectively. The strains were cultivated, FAMES and fatty alcohols analyzed as described in Example 3.

The presence of Ncb5or from *Agrotis segetum* and *Bombus terrestris* improved the activity of Desat70 in *Y. lipolytica* by 26.8 and 28.8%, respectively (Table 24). The activity of FAR1 reductase in *Y. lipolytica* improved by 25.8 and 0.65% when combined with Ncb5or from *Agrotis segetum* and *Bombus terrestris*, respectively (Table 25).

Table 24. Effect of Ncb5or from *Agrotis segetum* and *Bombus terrestris* on activity of desaturase Desat70 from *Cadra cautella*.

Strain	Genes expressed	Improvement purity (%)
ST12195	Desat70	Reference
ST12518	AseNcb5or Desat70	26.8
ST12519	BterNcb5or Desat70	28.2

Table 25. Effect of Ncb5or from *Agrotis segetum* and *Bombus terrestris* on activity of reductase FAR1 from *H. armigera*.

Strain	Genes expressed	Improvement in total fatty alcohol titer (%)
ST12118	FAR1	Reference
ST12395	AseNcb5or FAR1	25.8
ST12397	BterNcb5or FAR1	0.6

Sequence overview

Please note that SEQ ID NOs: 40, 43-74, 94-100, 104-110, 115-118, 125, 140-153, 168-180 and 186-189 have been codon optimized for *Yarrowia lipolytica*. SEQ ID NOs: 39, 75, 101-103 and 181 have been codon optimized for *Saccharomyces cerevisiae*.

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Desaturases

SEQ ID NO, Protein	SEQ ID NO, DNA	Name	Native to	Desaturase
1	39	Desat19	<i>Agrotis segetum</i>	$\Delta 11$ desaturase
2	40	Desat16	<i>Amyelois transitella</i>	$\Delta 11$ desaturase
3	41	Desat17	<i>Amyelois transitella</i>	$\Delta 9$ desaturase
4	42	Desat18	<i>Amyelois transitella</i>	$\Delta 9$ desaturase
5	43	Desat25	<i>Chauliognathus lugubris</i>	$\Delta 9$ desaturase
6	44	Desat47	<i>Chilo suppressalis</i>	Desaturase
7	45	Desat36	<i>Choristoneura parallela</i>	$\Delta 11$ desaturase
8	46	Desat35	<i>Choristoneura rosaceana</i>	$\Delta 11$ desaturase
9	47	Desat4	<i>Cydia pomonella</i>	Desaturase
10	48	Desat2	<i>Cydia pomonella</i>	Desaturase
11	49	Desat1	<i>Cydia pomonella</i>	Desaturase
12	50	Desat40	<i>Dendrolimus punctatus</i>	$\Delta 9$ desaturase
13	51	Desat59	<i>Drosophila grimshawi</i>	$\Delta 9$ desaturase
14	52	Desat24	<i>Drosophila melanogaster</i>	$\Delta 9$ desaturase
15	53	Desat61	<i>Drosophila virilis</i>	$\Delta 9$ desaturase
16	54	Desat33	<i>Epiphyas postvittana</i>	Desaturase
17	55	Desat31	<i>Grapholita molesta</i>	$\Delta 10$ desaturase
18	56	Desat55	<i>Grapholita molesta</i>	desaturase
19	57	Desat51	<i>Helicoverpa zea</i>	Desaturase
20	58	Desat30	<i>Lobesia botrana</i>	Desaturase

21	59	Desat43	<i>Lobesia botrana</i>	Desaturase
22	60	Desat52	<i>Manducta sexta</i>	$\Delta 11$ desaturase
23	61	Desat32	<i>Ostrinia nubilalis</i>	$\Delta 11$ desaturase
24	62	Desat48	<i>Pectinophora gossypiella</i>	$\Delta 11$ desaturase
25	63	Desat22	<i>Pelargonium hortorum</i>	$\Delta 9$ desaturase
26	64	Desat45	<i>Plutella xylostella</i>	$\Delta 11$ desaturase
27	65	Desat23	<i>Ricinus communis</i>	$\Delta 9$ desaturase
28	66	Desat42	<i>Saccharomyces cerevisiae</i>	$\Delta 9$ desaturase
29	67	Desat37	<i>Spodoptera exigua</i>	$\Delta 11$ desaturase
30	68	Desat20	<i>Spodoptera littoralis</i>	$\Delta 11$ desaturase
31	69	Desat20	<i>Spodoptera littoralis</i>	$\Delta 11$ desaturase
32	70	Desat38	<i>Spodoptera litura</i>	$\Delta 11$ desaturase
33	71	Desat26	<i>Spodoptera litura</i>	Desaturase
34	72	Desat34	<i>Thaumetopoea pityocampa</i>	$\Delta Z11-14$ desaturase
35	73	Desat28	<i>Tribolium castaneum</i>	Desaturase
36	74	Desat29	<i>Tribolium castaneum</i>	Desaturase
37	75	Desat21	<i>Trichoplusia ni</i>	$\Delta 11$ desaturase
38	76	Desat69	<i>Yarrowia lipolytica</i>	$\Delta 9$ desaturase
126	140	Desat72	<i>Antheraea pernyi</i>	$\Delta 11$ desaturase
127	141	Desat76	<i>Argyrotaenia velutinana</i>	$\Delta 11$ desaturase
128	142	Desat75	<i>Bombus lapidarius</i>	$\Delta 9$ desaturase
129	143	Desat78	<i>Bombyx mori</i>	$\Delta 11$ desaturase
130	144	Desat44	<i>Chilo suppressalis</i>	$\Delta 11$ desaturase
131	145	Desat60	<i>Drosophila ananassae</i>	$\Delta 9$ desaturase
132	146	Desat63	<i>Diatraea saccharalis</i>	Z11 desaturase
133	147	Desat56	<i>Drosophila yakuba</i>	$\Delta 9$ desaturase
134	148	Desat70	<i>Cadra cautella</i>	$\Delta 11$ desaturase
135	149	Desat71	<i>Lobesia botrana</i>	$\Delta 11$ desaturase

136	150	Desat77	<i>Ostrinia furnacalis</i>	Δ E14 desaturase
137	151	Desat65	<i>Plodia interpunctella</i>	Δ 11 desaturase
138	152	Desat27	<i>Tribolium castaneum</i>	Δ 9 desaturase
139	153	Desat73	<i>Yponomeuta padella</i>	Δ 11 desaturase

FARs

SEQ ID NO, Protein	SEQ ID NO, DNA	Name	Native to
77	94	FAR12	<i>Agrotis segetum</i>
78	95	FAR18	<i>Agrotis ipsilon</i>
79	96	FAR11	<i>Bicyclus anynana</i>
80	97	FAR14	<i>Bombus lapidarius</i>
81	98	FAR13	<i>Chilo suppressalis</i>
82	99	FAR23	<i>Cydia pomonella</i>
83	100	FAR1	<i>Helicoverpa armigera</i>
84	101	FAR6	<i>Helicoverpa assulta</i>
85	102	FAR4	<i>Heliothis subflexa</i>
86	103	FAR5	<i>Heliothis virescens</i>
87	104	FAR27	<i>Plutella xylostella</i>
88	105	FAR16	<i>Spodoptera exigua</i>
89	106	FAR22	<i>Spodoptera frugiperda</i>
90	107	FAR15	<i>Spodoptera littoralis</i>
91	108	FAR19	<i>Spodoptera litura</i>
92	109	FAR25	<i>Tyta alba</i>
93	110	FAR38	<i>Trichoplusia ni</i>
154	168	FAR33	<i>Amyelois transitella</i>
155	169	FAR34	<i>Amyelois transitella</i>
156	170	FAR35	<i>Amyelois transitella</i>
157	171	FAR47	<i>Chrysodeixis includens</i>
158	172	FAR46	<i>Cydia pomonella</i>
159	173	FAR42	<i>Marinobacter algicola</i>
160	174	FAR43	<i>Manducta sexta</i>
161	175	FAR44	<i>Ostrinia furnacalis</i>
162	176	FAR28	<i>Plodia interpunctella</i>

163	177	FAR30	<i>Plodia interpunctella</i>
164	178	FAR17	<i>Spodoptera exigua</i>
165	179	FAR45	<i>Spodoptera exigua</i>
166	180	FAR41	<i>Trichoplusia ni</i>
167	181	FAR8	<i>Yponomeuta rorellus</i>

Ncb5ors

SEQ ID NO, Protein	SEQ ID NO, DNA	Name	Native to
111	115	DgNcb5or	<i>Drosophila grimshawi</i>
112	116	DmNcb5or	<i>Drosophila melanogaster</i>
113	117	HsNcb5or	<i>Homo sapiens</i>
114	118	SlitNcb5or	<i>Spodoptera litura</i>
124	125	CpoNcb5or1	<i>Cydia pomonella</i>
182	186	CpNcb5or	<i>Cydia pomonella</i>
183	187	AseNcb5or	<i>Agrotis segetum</i>
184	188	BterNcb5or	<i>Bombus terrestris</i>
185	189	LboNcb5or	<i>Lobesia botrana</i>

Other

SEQ ID NO, Protein	Name	Native to
119	Fao1	<i>Yarrowia lipolytica</i>
120	GPAT	<i>Yarrowia lipolytica</i>
121	Hdf1	<i>Yarrowia lipolytica</i>
122	Hfd4	<i>Yarrowia lipolytica</i>
123	Pex10	<i>Yarrowia lipolytica</i>

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Cytochrome b5 and cytochrome b5 reductases

SEQ ID NO, Protein	Name	Native to
190	MaCytB5	<i>Mortierella alpina</i>
191	MaCytB5Red1	<i>Mortierella alpina</i>
192	MaCytB5Red2	<i>Mortierella alpina</i>

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Items

1. A cell expressing:
 - i) a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a desaturated fatty acyl-CoA and a desaturated fatty acid; and
 - ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);whereby the cell is capable of producing the compound with a higher titer compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.
2. A cell expressing
 - i) a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate and a desaturated fatty acyl-CoA; and
 - ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);whereby the cell is capable of producing the compound with a higher titer compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions.
3. The cell according to any one of items 1 or 2, wherein the first enzyme or group of enzymes comprises or consists of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA, whereby the cell is capable of producing a desaturated fatty acyl-CoA with a higher titer compared to a cell expressing said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.
4. The cell according to any one of items 1 or 2, wherein the first enzyme or group of enzymes comprises or consists of one or more fatty acyl reductase (FAR) capable of converting a fatty acyl-CoA to a fatty alcohol, whereby the cell is capable of producing a fatty alcohol with a higher titer compared to a cell expressing said one or more FAR but no heterologous Ncb5or when cultivated in the same conditions.

5. The cell according to any one of items 1 or 2, wherein the first enzyme or group of enzymes comprises or consists of one or more FAR and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol, whereby the cell is capable of producing a desaturated fatty alcohol with a higher titer compared to a cell expressing said one or more FAR and said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.
6. The cell according to any one of the preceding items, further expressing an acetyltransferase capable of converting a desaturated or a saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively, whereby the cell is capable of producing a desaturated or a saturated fatty alcohol acetate with a higher titer compared to a cell expressing the first group of enzymes and the acetyltransferase but no heterologous Ncb5or when cultivated in the same conditions.
7. The cell according to any one of the preceding items, wherein the Ncb5or is native to a plant, an insect or a mammal, such as *Homo sapiens*.
8. The cell according to any one of the preceding items, wherein the Ncb5or is native to an insect, such as an insect of the genus *Agrotis*, *Amyelois*, *Aphantopus*, *Arctia*, *Bicyclus*, *Bombyx*, *Bombus*, *Chilo*, *Cydia*, *Danaus*, *Drosophila*, *Eumeta*, *Galleria*, *Helicoverpa*, *Heliothis*, *Hyposmocoma*, *Leptidea*, *Lobesia*, *Manduca*, *Operophtera*, *Ostrinia*, *Papilio*, *Papilio*, *Papilio*, *Pieris*, *Plutella*, *Spodoptera*, *Trichoplusia*, and *Vanessa*.
9. The cell according to any one of the preceding items, wherein the Ncb5or is native to an insect selected from *Agrotis segetum*, *Amyelois transitella*, *Aphantopus hyperantus*, *Arctia plantaginis*, *Bicyclus anynana*, *Bombus terrestris*, *Bombyx mandarina*, *Bombyx mori*, *Chilo suppressalis*, *Cydia pomonella*, *Danaus plexippus*, *Drosophila grimshawi*, *Drosophila melanogaster*, *Eumeta japonica*, *Galleria mellonella*, *Helicoverpa armigera*, *Heliothis virescens*, *Hyposmocoma kahamanoa*, *Leptidea sinapis*, *Lobesia botrana*, *Manduca sexta*, *Operophtera brumata*, *Ostrinia furnacalis*, *Papilio machaon*,

Papilio polytes, *Papilio xuthus*, *Pieris rapae*, *Plutella xylostella*, *Spodoptera frugiperda*, *Spodoptera litura*, *Trichoplusia ni*, and *Vanessa tameamea*.

- 5 10. The cell according to any one of the preceding items, wherein the Ncb5or is selected from the group of Ncb5ors set forth in SEQ ID NOs: 111 to 114, SEQ ID NO: 124 and SEQ ID NO: 182 to 185, or variants having at least 70% identity thereto, such as at least 75% identity, such as at least 80% identity, such as at least 85% identity, such as at least 90% identity, such as at least 95% identity thereto.
- 10 11. The cell according to any one of the preceding items, wherein the Ncb5or is selected from:
 - 15 a. an Ncb5or from *Drosophila melanogaster* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Drosophila melanogaster* as set forth in SEQ ID NO: 112 (DmNcb5or) or a functional variant thereof having at least 80% identity thereto;
 - 20 b. an Ncb5or from *Spodoptera litura* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Spodoptera litura* (SlitNcb5or) as set forth in SEQ ID NO: 114 or a functional variant thereof having at least 80% identity thereto;
 - 25 c. an Ncb5or from *Drosophila grimshawi* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Drosophila grimshawi* as set forth in SEQ ID NO: 111 (DmNcb5or) or a functional variant thereof having at least 80% identity thereto;
 - 30 d. an Ncb5or from *Homo sapiens* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Homo sapiens* as set forth in SEQ ID NO: 113 (HsNcb5or) or a functional variant thereof having at least 80% identity thereto;
 - e. an Ncb5or from *Cydia pomonella* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Cydia pomonella* as set forth in SEQ ID NO: 124 (CpoNcb5or1) or SEQ ID NO: 182 (CpoNcb5or), or a functional variant thereof having at least 80% identity thereto;
 - 35 f. an Ncb5or from *Agrotis segetum* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Agrotis segetum* as set forth

- in SEQ ID NO: 183 (AseNcb5or) or a functional variant thereof having at least 80% identity thereto;
- g. an Ncb5or from *Bombus terrestris* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Bombus terrestris* as set forth in SEQ ID NO: 184 (BterNcb5or) or a functional variant thereof having at least 80% identity thereto; and
- h. an Ncb5or from *Lobesia botrana* or a variant thereof having at least 80% identity thereto, preferably the Ncb5or from *Lobesia botrana* as set forth in SEQ ID NO: 185 (LboNcb5or) or a functional variant thereof having at least 80% identity thereto.
12. The cell according to any one of the previous items, wherein the heterologous Ncb5or is one or more heterologous Ncb5ors, such as a plurality of different heterologous Ncb5ors.
13. The cell according to any one of the preceding items, wherein the desaturase is native to a plant, such as *Ricinus communis* or *Pelargonium hortorum*, or an insect, such as the *Diptera*, the *Coleoptera*, or the *Lepidoptera* order, such as of the genus *Agrotis*, *Antheraea*, *Argyrotaenia*, *Amyelois*, *Bombus*, *Bombyx*, *Cadra*, *Chauliognathus*, *Chilo*, *Choristoneura*, *Cydia*, *Dendrophilus*, *Diatraea*, *Drosophila*, *Ephestia*, *Epiphyas*, *Grapholita*, *Helicoverpa*, *Lampronia*, *Lobesia*, *Manducta*, *Ostrinia*, *Pectinophora*, *Plodia*, *Plutella*, *Thalassiosira*, *Thaumetopoea*, *Tribolium*, *Trichoplusia*, *Spodoptera* or *Yponomeuta*, such as *Agrotis segetum*, *Antheraea pernyi*, *Argyrotaenia velutiana*, *Amyelois transitella*, *Bombus lapidarius*, *Bombyx mori*, *Cadra cautella*, *Chauliognathus lugubris*, *Chilo suppressalis*, *Choristoneura parallela*, *Choristoneura rosaceana*, *Cydia pomonella*, *Dendrophilus punctatus*, *Diatraea saccharalis*, *Drosophila ananassae*, *Drosophila melanogaster*, *Drosophila virilis*, *Drosophila yakuba*, *Ephestia elutella*, *Ephestia kuehniella*, *Epiphyas postvittana*, *Grapholita molesta*, *Helicoverpa assulta*, *Helicoverpa zea*, *Lampronia capitella*, *Lobesia botrana*, *Manducta sexta*, *Ostrinia furnacalis*, *Ostrinia nubilalis*, *Pectinophora gossypiella*, *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*, *Spodoptera littoralis*, *Spodoptera litura*, *Thalassiosira pseudonana*, *Thaumetopoea pityocampa*, *Tribolium castaneum*, *Trichoplusia ni* or *Yponomeuta padella*.

14. The cell according to any one of the preceding items, wherein the desaturase is selected from the group consisting of a $\Delta 3$ desaturase, a $\Delta 5$ desaturase, a $\Delta 6$ desaturase, a $\Delta 7$ desaturase, a $\Delta 8$ desaturase, a $\Delta 9$ desaturase, a $\Delta 10$ desaturase, a $\Delta 11$ desaturase, a $\Delta 12$ desaturase, a $\Delta 13$ desaturase and a $\Delta 14$ desaturase, preferably wherein the desaturase is a $\Delta 9$ desaturase or a $\Delta 11$ desaturase.
15. The cell according to any one of the preceding items, wherein the desaturase is selected from the group of desaturases set forth in SEQ ID NOs: 1 to 38 and SEQ ID NOs: 126 to 139, or variants having at least 70% identity thereto, such as at least 75% identity, such as at least 80% identity, such as at least 85% identity, such as at least 90% identity, such as at least 95% identity.
16. The cell according to any one of the preceding items, wherein the desaturase is selected from:
- a *Spodoptera litura* desaturase, such as Desat38 as set forth in SEQ ID NO: 32;
 - a *Lobesia botrana* desaturase, such as Desat30 as set forth in SEQ ID NO: 20;
 - a *Drosophila virilis* desaturase, such as Desat61 as set forth in SEQ ID NO: 15;
 - a *Cadra cautella* desaturase, such as Desat70 as set forth in SEQ ID NO: 134;
 - a *Yarrowia lipolytica* desaturase, such as Desat69 as set forth in SEQ ID NO: 38;
 - an *Amyelois transitella* desaturase, such as Desat16 as set forth in SEQ ID NO: 2;
 - an *Agrotis segetum* desaturase, such as Desat19 as set forth in SEQ ID NO: 1;
 - a *Trichoplusia ni* desaturase, such as Desat21 as set forth in SEQ ID NO: 37;
 - a *Chilo suppressalis* desaturase, such as Desat44 as set forth in SEQ ID NO: 130;

- j. a *Plutella xylostella* desaturase, such as Desat45 as set forth in SEQ ID NO: 26;
- k. a *Spodoptera exigua* desaturase, such as Desat37 as set forth in SEQ ID NO: 29;
- 5 l. a *Diatraea saccharalis* Z11 desaturase, such as Desat63 as set forth in SEQ ID NO: 132;
- m. a *Plodia interpunctella* desaturase, such as Desat65 as set forth in SEQ ID NO: 137;
- 10 n. a *Lobesia botrana* desaturase, such as Desat71 as set forth in SEQ ID NO: 135;
- o. a *Antheraea pernyi* desaturase, such as Desat72 as set forth in SEQ ID NO: 126;
- p. a *Yponomeuta padella* desaturase, such as Desat73 as set forth in SEQ ID NO: 139;
- 15 q. a *Drosophila melanogaster* desaturase, such as Desat24 as set forth in SEQ ID NO: 14;
- r. a *Drosophila yakuba* desaturase, such as Desat56 as set forth in SEQ ID NO: 133;
- s. a *Drosophila grimshawi* desaturase, such as Desat59 as set forth in SEQ ID NO: 13;
- 20 t. a *Drosophila ananassae* desaturase, such as Desat60 as set forth in SEQ ID NO: 131;
- u. a *Drosophila virilis* desaturase, such as Desat61 as set forth in SEQ ID NO: 15;
- 25 v. a *Lobesia botrana* desaturase, such as Desat43 as set forth in SEQ ID NO: 21;
- w. a *Tribolium castaneum* desaturase, such as Desat27 as set forth in SEQ ID NO: 138;
- x. a *Bombus lapidarius* desaturase, such as Desat75 as set forth in SEQ ID NO: 128;
- 30 y. a *Lobesia botrana* desaturase, such as Desat30 as set forth in SEQ ID NO: 20;
- z. a *Choristoneura rosaceana* desaturase, such as Desat35 as set forth in SEQ ID NO: 8;

- aa. a *Choristoneura parallela* desaturase, such as Desat36 as set forth in SEQ ID NO: 7;
- bb. a *Manducta sexta* desaturase, such as Desat52 as set forth in SEQ ID NO: 22;
- 5 cc. a *Argyrotaenia velutinana* desaturase, such as Desat76 as set forth in SEQ ID NO: 127;
- dd. a *Ostrinia furnacalis* desaturase, such as Desat77 as set forth in SEQ ID NO: 136;
- ee. a *Bombyx mori* desaturase, such as Desat78 as set forth in SEQ ID NO: 129;
- 10 or a functional variant thereof having at least 80% sequence identity thereto.
17. The cell according to any one of the preceding items, wherein the FAR is native to an insect such as an insect of the *Lepidoptera* order, such as of the genus
- 15 *Agrotis*, *Amyelois*, *Bicyclus*, *Bombus*, *Chilo*, *Chrysodeixis*, *Cydia*, *Helicoverpa*, *Heliothis*, *Manducta*, *Ostrinia*, *Plodia*, *Plutella*, *Spodoptera*, *Trichoplusia*, *Tyta* or *Yponomeuta*, or wherein the FAR is native to a bacteria, such as of the genus *Marinobacter*.
- 20 18. The cell according to any one of the preceding items, wherein the FAR is a fatty acyl reductase native to *Agrotis segetum*, *Amyelois transitella*, *Bicyclus anynana*, *Bombus lapidaries*, *Chilo suppressalis*, *Chrysodeixis includes*, *Cydia pomonella*, *Helicoverpa armigera*, *Helicoverpa assulta*, *Heliothis virescens*, *Heliothis subflexa*, *Manducta sexta*, *Marinobacter algicola*, *Ostrinia furnacalis*,
- 25 *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*, *Spodoptera frugiperda*, *Spodoptera littoralis*, *Spodoptera litura*, *Trichoplusia ni*, *Tyta alba* or *Yponomeuta rorellus*, or a functional variant thereof having at least 80% identity thereto.
- 30 19. The cell according to any one of the preceding items, wherein the FAR is selected from the group of FARs set forth in SEQ ID NOs: 77 to 93 and SEQ ID NOs: 154 to 167, or variants having at least 70% identity thereto, such as at least 75% identity, such as at least 80% identity, such as at least 85% identity, such as at least 90% identity, such as at least 95% identity
- 35

20. The cell according to any one of the preceding items, wherein the FAR is selected from:

- a. a *Spodoptera littoralis* FAR, such as the FAR15 set forth in SEQ ID NO: 90;
- 5 b. a *Spodoptera exigua* FAR, such as the FAR as set forth in SEQ ID NO: 88 (FAR16);
- c. a *Helicoverpa armigera* FAR, such as the FAR as set forth in SEQ ID NO: 83 (FAR1);
- 10 d. an *Agrotis segetum* FAR, such as the FAR as set forth in SEQ ID NO: 77 (FAR12);
- e. a *Bicyclus anyana* FAR, such as the FAR as set forth in SEQ ID NO: 79 (FAR11);
- f. a *Cydia pomonella* FAR, such as the FAR as set forth in SEQ ID NO: 82 (FAR23);
- 15 g. a *Heliothis subflexa* FAR, such as the FAR as set forth in SEQ ID NO: 85 (FAR4)
- h. a *Helicoverpa assulta* FAR, such as the FAR as set forth in SEQ ID NO: 84 (FAR6);
- i. a *Tyta alba* FAR, such as the FAR as set forth in SEQ ID NO: 92 (FAR25);
- 20 j. a *Heliothis virescens* FAR, such as the FAR as set forth in SEQ ID NO: 86 (FAR5);
- k. a *Yponomeuta rorellus* FAR, such as the FAR as set forth in SEQ ID NO: 167 (FAR8);
- 25 l. a *Marinobacter algicola* FAR, such as the FAR as set forth in SEQ ID NO: (FAR159);
- m. a *Chilo suppressalis* FAR, such as the FAR as set forth in SEQ ID NO: 81 (FAR13);
- n. a *Spodoptera exigua* FAR, such as the FAR as set forth in SEQ ID NO: 164 (FAR17);
- 30 o. a *Agrotis ipsilon* FAR, such as the FAR as set forth in SEQ ID NO: 78 (FAR18);
- p. a *Plodia interpunctella* FAR, such as the FAR as set forth in SEQ ID NO: 162 (FAR28);

- q. a *Plodia interpunctella* FAR, such as the FAR as set forth in SEQ ID NO: 163 (FAR30);
- r. a *Manducta sexta* FAR, such as the FAR as set forth in SEQ ID NO: 160 (FAR43);
- 5 s. a *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 154 (FAR33);
- t. a *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 155 (FAR34);
- 10 u. a *Amyelois transitella* FAR, such as the FAR as set forth in SEQ ID NO: 156 (FAR35);
- v. a *Ostrinia furnacalis* FAR, such as the FAR as set forth in SEQ ID NO: 161 (FAR44);
- w. a *Spodoptera exigua* FAR, such as the FAR as set forth in SEQ ID NO: 165 (FAR45);
- 15 x. a *Trichoplusia ni* FAR, such as the FAR as set forth in SEQ ID NO: 166 (FAR41);
- y. a *Cydia pomonella* FAR, such as the FAR as set forth in SEQ ID NO: 158 (FAR46);
- 20 z. a *Chrysodeixis includens* FAR, such as the FAR as set forth in SEQ ID NO: 157 (FAR47);
- or a functional variant thereof having at least 80% identity thereto.
21. The cell according to any one of the preceding items, wherein at least one of the genes encoding a desaturase, a FAR, or an Ncb5or is present in high copy number.
- 25
22. The cell according to any one of the preceding items, wherein at least one of the genes encoding a desaturase, a FAR, or an Ncb5or is under the control of an inducible promoter.
- 30
23. The cell according to any one of the preceding items, wherein at least one of the genes encoding a desaturase, a FAR, or an Ncb5or is codon-optimized for said cell.

24. The cell according to any one of the preceding items, wherein the genes encoding a desaturase, a FAR, or an Ncb5or are each independently comprised within the genome of the cell or within a vector comprised within the cell.
- 5
25. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol, the saturated fatty alcohol, the desaturated fatty alcohol acetate, and/or the saturated fatty alcohol acetate have a carbon chain length of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22, preferably the carbon chain
- 10
- has a length of 11, 12, 13, 14, 15, 16, 17 or 18.
26. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol is desaturated in at least one position, such as at least two positions.
- 15
27. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol is desaturated at position 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21.
- 20
28. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol is selected from the group of desaturated fatty alcohols consisting of (Z)-9-tetradecen-1-ol (Z9-14:OH), (Z)-9-hexadecen-1-ol (Z9-16:OH), (Z)-11-tetradecen-1-ol (Z11-14:OH), (Z)-11-hexadecen-1-ol (Z11-16:OH), and codlemone (E8,E10-dodecadien-1-ol).
- 25
29. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol acetate is desaturated in at least one position, such as at least two positions.
- 30
30. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol acetate is desaturated at position 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21.
- 35
31. The cell according to any one of the preceding items, wherein the desaturated fatty alcohol acetate is *E8,E10*-dodecadienyl acetate.

32. The cell according to any one of the preceding items, wherein the cell expresses an Ncb5or selected from the group consisting of SEQ ID NOs: 111 to 114, SEQ ID NO: 124 and SEQ ID NOs: 182 to 185, and
- 5 a. a desaturase selected from the group consisting of SEQ ID NOs: 1 to 38 and SEQ ID NOs: 126 to 139, and a FAR selected from the group consisting of SEQ ID NOs: 77 to 93 and SEQ ID NOs 154 to 167;
 - b. a desaturase from *Spodoptera litura* (Desat38) as set forth in SEQ ID NO: 32, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in
10 SEQ ID NO: 83; or
 - c. a desaturase from *Lobesia botrana* (Desat30) as set forth in SEQ ID NO: 20, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in
 SEQ ID NO: 83; or
 - d. a desaturase from *Drosophila virilis* (Desat61) as set forth in SEQ ID
15 NO: 15, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in
 SEQ ID NO: 83;
- or functional variants thereof having at least 80% identity thereto.
33. The cell according to any one of the preceding items, wherein the cell expresses:
- 20 a. a *Spodoptera litura* desaturase such as Desat38 as set forth in SEQ ID NO: 32; a *Helicoverpa armigera* FAR such as FAR1 as set forth in SEQ ID NO: 83; and an Nc5bor selected from the group consisting of a *Drosophila melanogaster* Ncb5or, such as DmNcb5or as set forth in SEQ ID NO: 112,
25 and a *Spodoptera litura* Ncb5or such as SlitNcb5or as set forth in SEQ ID NO: 114; or
 - b. a *Lobesia botrana* desaturase such as Desat30 as set forth in SEQ ID NO: 20; a *Helicoverpa armigera* FAR such as FAR1 as set forth in SEQ ID NO: 83; and an Nc5bor selected from the group consisting of a *Drosophila melanogaster* Ncb5or such as DmNcb5or as set forth in SEQ ID NO: 112, a
30 *Spodoptera litura* Ncb5or such as SlitNcb5or as set forth in SEQ ID NO: 114, a *Drosophila grimshawi* Ncb5or such as DgNcb5or as set forth in SEQ ID NO: 111, and a *Homo sapiens* Ncb5or such as HsNcb5or as set forth in
 SEQ ID NO:113; or

- 5 c. a *Drosophila virilis* desaturase such as Desat61 as set forth in SEQ ID NO: 15; a *Helicoverpa armigera* FAR such as FAR1 as set forth in SEQ ID NO: 83; and an Ncb5or selected from the group consisting of a *Drosophila melanogaster* Ncb5or such as DmNcb5or as set forth in SEQ ID NO: 112, and a *Drosophila grimshawi* Ncb5or such as DgNcb5or as set forth in SEQ ID NO: 111.
- 10 34. The cell according to any one of the preceding items, wherein said cell is a yeast cell, preferably an oleaginous yeast cell.
- 15 35. The yeast cell according to item 34, wherein the genus of said yeast cell is selected from the group consisting of *Saccharomyces*, *Pichia*, *Yarrowia*, *Kluyveromyces*, *Candida*, *Rhodotorula*, *Rhodospiridium*, *Cryptococcus*, *Trichosporon* and *Lipomyces*.
- 20 36. The yeast cell according to any one of items 34 to 35, wherein the yeast is selected from the group consisting of *Saccharomyces cerevisiae*, *Saccharomyces boulardi*, *Pichia pastoris*, *Kluyveromyces marxianus*, *Candida tropicalis*, *Cryptococcus albidus*, *Lipomyces lipofera*, *Lipomyces starkeyi*, *Rhodospiridium toruloides*, *Rhodotorula glutinis*, *Trichosporon pullulan* and *Yarrowia lipolytica*.
- 25 37. The cell according to any one of items 1 to 33, wherein said cell is a plant cell.
- 30 38. The plant cell according to item 37, wherein the genus of said plant is selected from the group consisting of *Nicotiana* and *Camelina*.
39. The plant cell according to any one items 37 to 38, wherein said plant is selected from the group consisting of *Nicotiana tabacum*, *Nicotiana benthamiana*, and *Camelina sativa*.
40. A method for increasing the activity of at least one enzyme selected from the group consisting of desaturases and fatty acyl CoA reductases (FARs), said method comprising the steps of:

- 5 a. providing a desaturase capable of introducing at least one double bond
in a fatty acyl-CoA, thereby converting at least part of said fatty acyl-
CoA to a desaturated fatty-acyl-CoA; and/or
- b. providing a FAR capable of converting at least part of said desaturated
fatty acyl-CoA to a desaturated fatty alcohol, thereby producing said
desaturated fatty alcohol; and
- c. contacting said desaturase and/or FAR with an Ncb5or, thereby
increasing the activity of said desaturase and/or FAR compared to the
activity of said desaturase and/or FAR in the absence of said Ncb5or,
10 wherein the activity is measured under the same conditions;
wherein the increase in activity is measured by measuring the concentration of
product formed by the desaturase and/or the FAR.
- 15 41. The method according to item 40, wherein the method is performed in vitro.
42. The method according to item 40, wherein the method is performed in vivo,
preferably wherein the method is performed in:
- a. a yeast cell according to any one of items 34 to 36; or
- b. a plant cell according to any one of items 37 to 39.
- 20 43. A method for production of a compound selected from a desaturated fatty
alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a
desaturated fatty acid and a desaturated fatty acyl-CoA in a cell, said method
comprising the steps of:
- 25 a. providing a cell and incubating said cell in a medium; and
- b. expressing in said cell a first enzyme or group of enzymes capable of
converting a fatty acyl-CoA to said compound, thereby converting at
least part of said fatty acyl-CoA to said compound; and
- c. expressing in said cell an Ncb5or;
- 30 d. optionally, recovering said compound.
44. A method for increasing the titer of a compound selected from a desaturated
fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a
desaturated fatty acid and a desaturated fatty acyl-CoA produced in a cell
35 capable of synthesising one or more fatty acyl-CoAs and/or capable of

importing fatty acyl-CoAs from its environment, said method comprising the steps of:

- 5 a. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
 - b. expressing in said cell an Ncb5or, thereby increasing the titer of said compound compared to the titer from a cell not expressing said Ncb5or in the same conditions;
 - 10 c. optionally, recovering said compound.
45. The method according to any one of items 43 to 44, wherein the first enzyme or group of enzymes consists of one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA and wherein said compound is a desaturated fatty acyl-CoA or a desaturated fatty acid.
- 15 46. The method according to any one of items 43 to 44, wherein the first enzyme or group of enzymes consists of one or more FAR capable of converting a fatty acyl-CoA to a saturated fatty alcohol and wherein said compound is a saturated fatty alcohol.
- 20 47. The method according any one of items 43 to 44, wherein the first enzyme or group of enzymes consists of one or more FAR and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol and wherein said compound is a desaturated fatty alcohol.
- 25 48. The method according to any one of items 43 to 47, wherein the compound is a desaturated or a saturated fatty alcohol and wherein the method further comprises the step of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively.
- 30 49. The method according to item 48, wherein the conversion of the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate is performed in vitro.

50. The method according to item 48, wherein the conversion of the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate is performed in vivo by further expressing in the cell an acetyltransferase capable of converting the desaturated or the saturated fatty alcohol to a desaturated or a saturated fatty alcohol acetate, respectively.
51. The method according to any one of items 43 to 50, wherein said compound is a saturated fatty alcohol or a desaturated fatty alcohol, and wherein the method further comprises a step of converting the saturated fatty alcohol or the desaturated fatty alcohol to a saturated fatty aldehyde or to a desaturated fatty aldehyde, respectively.
52. The method according to item 51, wherein the conversion to an aldehyde is a chemical conversion or an enzymatic conversion.
53. The method according to any one of items 43 to 52, wherein the cell is a yeast cell as defined in any one of items 34 to 36.
54. The method according to any one of items 43 to 53, wherein the total titer of fatty alcohols and optionally the total titer of fatty alcohol acetates is increased, wherein the total titer of fatty alcohols is the sum of the titer of desaturated fatty alcohols and the titer of saturated fatty alcohols, and the total titer of fatty alcohol acetates is the sum of the titer of desaturated fatty alcohol acetates and the titer of saturated fatty alcohol acetates.
55. The method according to any one of items 43 to 54, wherein the titer of saturated fatty alcohols and optionally the titer of saturated fatty alcohol acetates is increased.
56. The method according to any one of items 43 to 55, wherein the titer of desaturated fatty alcohols and/or fatty alcohol acetates and/or fatty acids and/or saturated fatty alcohols and/or fatty alcohol acetates and/or the total titer of saturated fatty alcohols and/or fatty alcohol acetates is increased at least 3% compared to the titer from a cell not expressing said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at

least 20%, such as at least 25%, such as at least 30%, such as at least 35%,
such as at least 40%, such as at least 45%, such as at least 50%, such as at
least 55%, such as at least 60%, such as at least 70%, such as at least 80%,
such as at least 90%, such as at least 100%, such as at least 150%, such as at
5 least 200%, such as at least 250%.

57. The method according to any one of items 40 to 56, wherein the desaturase is
as defined in any one of items 13 to 16.
- 10 58. The method according to any one of items 40 to 57, wherein the FAR is as
defined in any one of items 17 to 20.
59. The method according to any one of items 40 to 58, wherein the Ncb5or is as
defined in any one of items 7 to 12.
- 15 60. The method according to any one of items 40 to 59, wherein the desaturated
fatty alcohol, the saturated fatty alcohol, the desaturated fatty alcohol acetate
and/or the saturated fatty alcohol acetate is as defined in item 25.
- 20 61. The method according to any one of items 40 to 60, wherein the desaturated
fatty alcohol is as defined in any one of items 26 to 28.
62. The method according to any one of items 40 to 61, wherein the desaturated
fatty alcohol acetate is as defined in any one of items 29 to 31.
- 25 63. The method according to any one of items 40, 42 to 44, and 54 to 62, wherein
the cell is a plant cell is as defined in any one of items 37 to 39.
64. The method according to any one of items 40 to 63, further comprising the step
30 of formulating the desaturated fatty alcohol, the desaturated fatty alcohol
acetate, and/or the desaturated fatty aldehyde in a pheromone composition.
65. The method according to item 64, wherein the pheromone composition further
comprises one or more additional compounds such as a liquid or solid carrier or
35 substrate.

66. The method according to any one of items 40 to 65, wherein the method yields said desaturated fatty alcohol, saturated fatty alcohol, desaturated fatty alcohol acetate, saturated fatty alcohol acetate, desaturated fatty aldehyde, and/or saturated fatty aldehyde with a titer of at least 1 mg/L, such as at least 1.5 mg/L, such as at least 5 mg/L, such as at least 10 mg/L, such as at least 25 mg/L, such as at least 50 mg/L, such as at least 100 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at least 750 mg/L, such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L, such as at least 4 g/L, such as at least 5 g/L, such as at least 6 g/L, such as at least 7 g/L, such as at least 8 g/L, such as at least 9 g/L, such as at least 10 g/L, such as at least 11 g/L, such as at least 12 g/L, such as at least 13 g/L, such as at least 14 g/L, such as at least 15 g/L, such as at least 16 g/L, such as at least 17 g/L, such as at least 18 g/L, such as at least 19 g/L, such as at least 20 g/L, such as at least 25 g/L, such as at least 30 g/L, such as at least 35 g/L, such as at least 40 g/L, such as at least 45 g/L, such as at least 50 g/L, or more.
67. The method according to any one of items 40 to 66, further comprising converting the saturated fatty alcohol or the desaturated fatty alcohol to a saturated fatty aldehyde or to a desaturated fatty aldehyde, respectively, by expression of at least one alcohol dehydrogenase and/or at least one fatty alcohol oxidase in said yeast cell.
68. A system of nucleic acid constructs comprising nucleic acids encoding an Ncb5or and:
- a desaturase capable of introducing at least one double bond in a fatty acyl-CoA; and/or
 - a fatty acyl CoA reductase (FAR) capable of converting at least part of a desaturated fatty acyl-CoA to a desaturated fatty alcohol.
69. The system according to item 68, wherein the Ncb5or is encoded by any one of the sequences set forth in SEQ ID NOs: 115 to 118, SEQ ID NO: 125 and SEQ ID NOs: 186 to 189, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, such

as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.

- 5 70. The system according to any one of items 68 to 69, wherein the desaturase is encoded by any one of the sequences set forth in SEQ ID NOs: 39 to 76 and SEQ ID NOs: 140 to 153, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, 10 such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.
- 15 71. The system according to any one of items 68 to 70, wherein the FAR is encoded by any one of the sequences set forth in SEQ ID NOs: 94 to 110 and SEQ ID NOs: 168 to 181, or variants thereof having at least 80% identity thereto, such as at least 85% identity, such as at least 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, 20 such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity thereto.
- 25 72. A kit of parts comprising:
a. the cell according to any one of items 1 to 33; and/or
b. the nucleic acid system according to any one of items 68 to 71, wherein said construct is for modifying a cell; and
c. instructions for use; and
d. optionally the cell to be modified.
- 30 73. The kit of parts according to item 72, wherein the cell is a yeast cell according to any one of items 34 to 36.
- 35 74. The kit of parts according to item 72, wherein the cell is a plant cell according to any one of items 37 to 39.

75. Use of an Ncb5or in a method for increasing the activity of one or more enzymes.
- 5 76. The use according to item 75, wherein the one or more enzymes is one or more membrane-bound enzymes.
77. The use according to any one of items 75 to 76, wherein the one or more enzymes is selected from the group consisting of desaturases and reductases.
- 10 78. The use according any one of items 75 to 77, wherein the increase in activity of said of one or more enzymes is at least 1.2-fold for the desaturase and/or the FAR, such as at least 1.3-fold, such as at least 1.4-fold, such as at least 1.5-fold, such as at least 1.6-fold, such as at least 1.7-fold, such as at least 1.8-fold, such as at least 1.9-fold, such as at least 2-fold, such as at least 3-fold, such as at least 4-fold, such as at least 5-fold, such as at least 6-fold, such as at least 7-fold, such as at least 8-fold, such as at least 9-fold, such as at least 10-fold, such as at least 15-fold, such as at least 20-fold, such as at least 30-fold, such as at least 40-fold, such as at least 50-fold; wherein the increase in activity of said of one or more enzymes is compared to the activity of said one or more enzymes in the absence of said Ncb5or, wherein the activity is measured under the same conditions, wherein the increase is measured by measuring the concentration of product formed by the one or more enzymes.
- 15 20
- 25 79. The use according to any one of items 75 to 78, wherein the increase in activity of said of one or more enzymes is at least 1.2-fold for the desaturase and/or the FAR, such as at least 1.3-fold, such as at least 1.4-fold, such as at least 1.5-fold, such as at least 1.6-fold, such as at least 1.7-fold, such as at least 1.8-fold, such as at least 1.9-fold, such as at least 2-fold, such as at least 3-fold, such as at least 4-fold, such as at least 5-fold, such as at least 6-fold, such as at least 7-fold, such as at least 8-fold, such as at least 9-fold, such as at least 10-fold, such as at least 15-fold, such as at least 20-fold, such as at least 30-fold, such as at least 40-fold, such as at least 50-fold; wherein the increase in activity of said of one or more enzymes is compared to the activity of said one or more enzymes in the absence of said Ncb5or, wherein the activity is measured under
- 30

the same conditions, wherein the increase is measured by measuring the concentration of product formed by the desaturase and/or the FAR.

- 5 80. The use according to any one of items 75 to 79, wherein the Ncb5or, the desaturase and/or the FAR are as defined in any one of the preceding claims.
- 10 81. The use according to any one of items 75 to 80, wherein the Ncb5or is selected from the group consisting of SEQ ID NOs: 111 to 114, SEQ ID NO: 124 and SEQ ID NO: 182 to 185.
- 15 82. The use according to any one of items 75 to 81, wherein the one or more enzymes is selected from the group consisting of SEQ ID NOs: 1 to 38, SEQ ID NOs: 77 to 93, SEQ ID NOs: 140 to 153 and SEQ ID NOs: 168 to 181.
- 20 83. The use according to any one of items 75 to 82, wherein the one or more enzymes is selected from:
- a. a desaturase from *Spodoptera litura* (Desat38) as set forth in SEQ ID NO: 32, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83; or
 - 25 b. a desaturase from *Lobesia botrana* (Desat30) as set forth in SEQ ID NO: 20, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83; or
 - c. a desaturase from *Drosophila virilis* (Desat61) as set forth in SEQ ID NO: 15, and a FAR from *Helicoverpa armigera* (FAR1) as set forth in SEQ ID NO: 83;
- or functional variants thereof having at least 80% identity thereto.
- 30 84. The use according to any one of items 75 to 83, wherein the Nc5bor is selected from the group consisting of a *Drosophila melanogaster* Ncb5or, such as DmNcb5or as set forth in SEQ ID NO: 112; a *Spodoptera litura* Ncb5or such as SlitNcb5or as set forth in SEQ ID NO: 114; a *Drosophila grimshawi* Ncb5or such as DgNcb5or as set forth in SEQ ID NO: 111; a *Homo sapiens* Ncb5or such as HsNcb5or as set forth in SEQ ID NO: 113; a *Cydia pomonella* Ncb5or such as CpoNcb5or1 as set forth in SEQ ID NO: 124 or CpNcb5or as set forth
- 35 in SEQ ID NO: 182; an *Agrotis segetum* Ncb5or such as AseNcb5or as set forth

in SEQ ID NO: 183; a *Bombus terrestris* Ncb5or such as BterNcb5or as set forth in SEQ ID NO: 184; a *Lobesia botrana* Ncb5or such as LboNcb5or as set forth in SEQ ID NO: 185; or functional variants thereof having at least 80% identity thereto.

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85. A desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde and/or a saturated fatty aldehyde obtainable by the method according to any one of items 40 to 67.

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86. Use of a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde and/or a saturated fatty aldehyde obtainable by the method according to any one of items 40 to 67.

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87. A method of monitoring the presence of pest or disrupting the mating of pest, said method comprising the steps of:

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- a. producing a desaturated fatty alcohol and optionally a desaturated fatty alcohol acetate and/or a desaturated fatty aldehyde according to the method of any one of items 40 to 67; and
- b. formulating said fatty alcohol and optionally said fatty alcohol acetate and/or said desaturated fatty aldehyde as a pheromone composition; and
- c. employing said pheromone composition as an integrated pest management composition.

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88. A fermentation broth containing the yeast cell according to any one of items 34 to 36.

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89. A fermentation system or a catalytic system comprising the yeast cell according to any one of items 34 to 36.

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90. A device, such as a pheromone dispenser, for diffusing a pheromone composition, said pheromone composition comprising the desaturated fatty alcohol and/or the desaturated fatty alcohol acetate and/or the desaturated fatty aldehyde according to any one of items 25 to 31 or 85.

91. A method for producing at least 1 mg/L of a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, a saturated fatty alcohol acetate, a desaturated fatty aldehyde and/or a saturated fatty aldehyde in a cell, such as at least 1.5 mg/L, such as at least 5 mg/L, such as at least 10 mg/L, such as at least 25 mg/L, such as at least 50 mg/L, such as at least 100 mg/L, such as at least 250 mg/L, such as at least 500 mg/L, such as at least 750 mg/L, such as at least 1 g/L, such as at least 2 g/L, such as at least 3 g/L, such as at least 4 g/L, such as at least 5 g/L, such as at least 6 g/L, such as at least 7 g/L, such as at least 8 g/L, such as at least 9 g/L, such as at least 10 g/L, such as at least 11 g/L, such as at least 12 g/L, such as at least 13 g/L, such as at least 14 g/L, such as at least 15 g/L, such as at least 16 g/L, such as at least 17 g/L, such as at least 18 g/L, such as at least 19 g/L, such as at least 20 g/L, such as at least 25 g/L, such as at least 30 g/L, such as at least 35 g/L, such as at least 40 g/L, such as at least 45 g/L, such as at least 50 g/L, or more, wherein the method is according to any one of items 40 to 67.
92. The method according to any one of items 43 to 67 or 91, wherein the medium comprises an extractant in an amount equal to or greater than its cloud concentration in an aqueous solution, wherein the extractant a non-ionic surfactant such as an antifoaming agent, preferably a polyethoxylated surfactant selected from: a polyethylene polypropylene glycol, a mixture of polyether dispersions, an antifoaming agent comprising polyethylene glycol monostearate such as simethicone and ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agents and combinations thereof.
93. The method according to item 92, wherein:
- the non-ionic surfactant is an ethoxylated and propoxylated C₁₆-C₁₈ alcohol-based antifoaming agent, such as C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate (CAS number 68002-96-0), and wherein the culture medium comprises at least 1% vol/vol of C₁₆-C₁₈ alkyl alcohol ethoxylate propoxylate,
 - the non-ionic surfactant is a polyethylene polypropylene glycol, for example Kolliphor® P407 (CAS number 9003-11-6), and wherein the culture medium comprises at least 10% vol/vol of polyethylene polypropylene glycol such as Kolliphor® P407,

- the non-ionic surfactant is a mixture of polyether dispersions, such as antifoam 204, and wherein the culture medium comprises at least 1% vol/vol of a mixture of polyether dispersions such as antifoam 204; and/or
 - the non-ionic surfactant is a non-ionic surfactant comprising polyethylene glycol monostearate such as simethicone, and wherein the culture medium comprises at least 1% vol/vol of polyethylene glycol monostearate or simethicone.
94. The method according to any one of items 43 to 67 or 91 to 93, wherein the culture medium comprises the extractant in an amount greater than its cloud concentration by at least 50%, such as at least 100%, such as at least 150%, such as at least 200%, such as at least 250%, such as at least 300%, such as at least 350%, such as at least 400%, such as at least 500%, such as at least 750%, such as at least 1000%, or more, and/or wherein the culture medium comprises the extractant in an amount at least 2-fold its cloud concentration, such as at least 3-fold its cloud concentration, such as at least 4-fold its cloud concentration, such as at least 5-fold its cloud concentration, such as at least 6-fold its cloud concentration, such as at least 7-fold its cloud concentration, such as at least 8-fold its cloud concentration, such as at least 9-fold its cloud concentration, such as at least 10-fold its cloud concentration, such as at least 12.5-fold its cloud concentration, such as at least 15-fold its cloud concentration, such as at least 17.5-fold its cloud concentration, such as at least 20-fold its cloud concentration, such as at least 25-fold its cloud concentration, such as at least 30-fold its cloud concentration.
95. The method according to any one of items 43 to 67 and 91 to 94, wherein the cell is a yeast cell and wherein:
- a. the desaturated fatty alcohol is (Z)-11-hexadecen-1-ol; and
 - b. the desaturase is a $\Delta 11$ -desaturase selected from the group consisting of the *Amyelois transitella* $\Delta 11$ -desaturase (Desat16; SEQ ID NO: 2), the *Spodoptera littoralis* $\Delta 11$ -desaturase (Desat20; SEQ ID NO: 31), the *Agrotis segetum* $\Delta 11$ -desaturase (Desat19; SEQ ID NO: 1) and the *Trichoplusia ni* $\Delta 11$ -desaturase (Desat21; SEQ ID NO: 37) or a variant thereof having at least 65% identity, such as at least 70% identity, such as at least 71% identity, such as at least 72%, such as at least 73%, such as at least 74%, such as at least 75%, such as at least 80%, such

as at least 85%, such as at least 90%, such as at least 95%, such as 100% identity to Desat16 (SEQ ID NO: 2), Desat20 (SEQ ID NO: 31), Desat19 (SEQ ID NO: 1), or Desat21 (SEQ ID NO: 37); and

- 5 c. the FAR is selected from the group consisting of FAR1 (SEQ ID NO: 83), FAR4 (SEQ ID NO: 85), and FAR6 (SEQ ID NO: 84), or a variant thereof having at least 80% identity, such as at least 85%, such as at least 90%, such as at least 95%, such as 100% identity to FAR1 (SEQ ID NO: 83), FAR4 (SEQ ID NO: 85), or FAR6 (SEQ ID NO: 84);
- 10 wherein said Δ 11-desaturase is capable of converting at least part of hexadecanoyl-CoA to (Z)11-hexadecenoyl-CoA, and said FAR is capable of converting at least part of (Z)11-hexadecenoyl-CoA to (Z)-11-hexadecenol, thereby obtaining (Z)-11-hexadecen-1-ol with a titre of at least 0.2 mg/L.

- 15 96. The yeast cell according to any one of items 34 to 36, wherein said yeast cell is an oleaginous yeast cell, wherein said oleaginous yeast cell has a mutation resulting in reduced activity of the fatty alcohol oxidase Fao1 (SEQ ID NO: 119) and a mutation resulting in reduced activity of at least one of the fatty aldehyde dehydrogenase Hfd1 (SEQ ID NO: 121), the fatty aldehyde dehydrogenase Hfd4 (SEQ ID NO: 122), the peroxisome biogenesis factor Pex10 (SEQ ID NO: 123), and the glycerol-3-phosphate acyltransferase GPAT (SEQ ID NO: 120), or
- 20 having a mutation resulting in reduced activity of at least one protein having at least 60% identity to Fao1 (SEQ ID NO: 119) and a mutation resulting in reduced activity of at least one of Hfd1 (SEQ ID NO: 121), Hfd4 (SEQ ID NO: 122), Pex10 (SEQ ID NO: 123) and GPAT (SEQ ID NO: 120), such as at least
- 25 65% identity, such as at least 70% identity, such as at least 75% identity, such as at least 80% identity, such as at least 81% identity, such as at least 82% identity, such as at least 83% identity, such as at least 84% identity, such as at least 85% identity, such as at least 86% identity, such as at least 87% identity, such as at least 88% identity, such as at least 89% identity, such as at least
- 30 90% identity, such as at least 91% identity, such as at least 92% identity, such as at least 93% identity, such as at least 94% identity, such as at least 95% identity, such as at least 96% identity, such as at least 97% identity, such as at least 98% identity, such as at least 99% identity to Fao1 (SEQ ID NO: 119) and at least one of Hfd1 (SEQ ID NO: 121), Hfd4 (SEQ ID NO: 122), Pex10 (SEQ
- 35 ID NO: 123) and GPAT (SEQ ID NO: 120), preferably wherein the yeast cell

has at least a mutation resulting in reduced activity of Fao1 and at least one mutation resulting in reduced activity of Hfd1, Hfd4, Pex10 and GPAT.

- 5 97. The yeast cell according to any one of items 34 to 36, wherein said yeast cell expresses a desaturase which has a higher specificity towards tetradecanoyl-CoA than towards hexadecanoyl-CoA and/or wherein the FAR has a higher specificity towards desaturated tetradecanoyl-CoA than towards desaturated hexadecanoyl-CoA.
- 10 98. The yeast cell according to any one of items 34 to 36, wherein said yeast cell:
- a. has one or more mutations resulting in reduced activity of one or more native acyl-CoA oxidases; and
 - b. expresses at least one first group of enzymes comprising at least one acyl-CoA oxidase capable of oxidising a fatty acyl-CoA, wherein the first group of enzymes is capable of shortening a fatty acyl-CoA of a first carbon chain length X to a shortened fatty acyl-CoA having a second carbon chain length X', wherein $X' \leq X-2$; and
 - 15 c. expresses at least one heterologous desaturase capable of introducing at least one double bond in said fatty acyl-CoA and/or in said shortened fatty acyl-CoA; and
 - 20 d. expresses at least one heterologous FAR, capable of converting at least part of said desaturated fatty acyl-CoA to a desaturated fatty alcohol; and
 - e. optionally expresses at least one acetyltransferase capable of
 - 25 converting at least part of said desaturated fatty alcohol to a desaturated fatty alcohol acetate, and/or at least one alcohol dehydrogenase and/or fatty alcohol oxidase capable of converting at least part of said desaturated fatty alcohol to a desaturated fatty aldehyde.
- 30 99. The yeast cell according to any one of items 34 to 36, wherein said yeast cell is capable of producing *E8,E10*-dodecadienyl coenzyme A and optionally *E8,E10*-dodecadien-1-ol, said yeast cell expressing at least one heterologous desaturase capable of introducing one or more double bonds in a fatty acyl-CoA having a carbon chain length of 12, thereby converting said fatty acyl-CoA to a

desaturated fatty acyl-CoA, wherein at least part of said desaturated fatty acyl-CoA is *E8,E10*-dodecadienyl coenzyme A (*E8,E10*-C12:CoA), wherein:

- 5 a. the at least one desaturase is Desat4 (SEQ ID NO: 9), or a functional variant thereof having at least 80% identity thereto, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to SEQ ID NO: 9; or
- 10 b. the at least one desaturase is at least two desaturases, wherein at least one of said two desaturases is Desat4 (SEQ ID NO: 9), or a functional variant thereof having at least 80% identity thereto, such as at least 81%, such as at least 82%, such as at least 83%, such as at least 84%, such as at least 85%, such as at least 86%, such as at least 87%, such as at least 88%, such as at least 89%, such as at least 90%, such as at least 91%, such as at least 92%, such as at least 93%, such as at least 94%, such as at least 95%, such as at least 96%, such as at least 97%, such as at least 98%, such as at least 99% identity to SEQ ID NO: 9, and the other desaturase is
- 15 a desaturase capable of introducing at least one double bond in a fatty acyl-CoA having a carbon chain length of 12, such as a Z9-12 desaturase.
- 20

100. A method for increasing the purity of a compound selected from a a desaturated fatty alcohol, a desaturated fatty acid and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:

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- 30 a. expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
- 35 b. expressing in said cell an Ncb5or, thereby increasing the production of said compound compared to the production from a cell not expressing said Ncb5or in the same conditions;
- wherein the purity of said compound is the ratio or percentage of said compound in relation to all compounds within the same compound group

5 produced by the cell, such as the percentage of said desaturated fatty alcohol in relation to all desaturated fatty alcohols produced by the cell, such as the percentage of desaturated fatty acid in relation to all fatty acids produced by the cell, and/or such as the percentage of desaturated fatty acyl-CoA in relation to all fatty acyl-CoA produced by the cell.

10 101. The method according to item 100, wherein the purity of desaturated fatty alcohol, desaturated fatty acid and/or desaturated fatty acyl-CoA is increased at least 3% compared to the purity from a cell not expressing said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such as at least 55%, such as at least 60%, such as at least 70%, such as at least 80%, such as at least 90%, such as at least 100%, such as at least 150%,
15 such as at least 200%, such as at least 250%.

102. The method according to any one of items 100 to 101, wherein the first enzyme or group of enzymes comprises
a. a desaturase as defined in any one of items 13 to 16; and/or
20 b. a FAR as defined in any one of items 17 to 20.

103. The method according to any one of items 100 to 102, wherein the Ncb5or is as defined in any one of items 7 to 12.

25 104. The method according to any one of items 100 to 103, wherein the cell is a yeast, wherein the genus of said yeast cell is selected from the group consisting of *Saccharomyces*, *Pichia*, *Yarrowia*, *Kluyveromyces*, *Candida*, *Rhodotorula*, *Rhodospiridium*, *Cryptococcus*, *Trichosporon* and *Lipomyces*, such as a yeast selected from the group consisting of *Saccharomyces cerevisiae*, *Saccharomyces boulardi*, *Pichia pastoris*, *Kluyveromyces marxianus*, *Candida tropicalis*, *Cryptococcus albidus*, *Lipomyces lipofera*,
30 *Lipomyces starkeyi*, *Rhodospiridium toruloides*, *Rhodotorula glutinis*, *Trichosporon pullulan* and *Yarrowia lipolytica*.

105. The method according to any one of items 100 to 103, wherein the cell is a plant cell, wherein the genus of said plant is selected from the group consisting of *Nicotiana* and *Camelina*, such as a plant selected from the group consisting of *Nicotiana tabacum*, *Nicotiana benthamiana*, and *Camelina sativa*.

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106. The method according to any one of items 100 to 105, wherein the compound:

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- a. has a carbon chain length of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22, preferably the carbon chain has a length of 11, 12, 13, 14, 15, 16, 17 or 18;
 - b. is desaturated at position 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21;
 - c. is desaturated in at least one position, such as at least two positions; and/or
 - 15 d. is selected from the group consisting of Z9-14:acid, Z9-16:acid, Z11-14:acid, Z11-16:acid, E8,E10-12:acid, of (Z)-9-tetradecen-1-ol (Z9-14:OH), (Z)-9-hexadecen-1-ol (Z9-16:OH), (Z)-11-tetradecen-1-ol (Z11-14:OH), (Z)-11-hexadecen-1-ol (Z11-16:OH), and codlemone (E8,E10-dodecadien-1-ol).

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Claims

1. A cell expressing:
 - i) a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate and a desaturated fatty acyl-CoA; and
 - ii) a heterologous NAD(P)H cytochrome b5 oxidoreductase (Ncb5or);whereby the cell is capable of producing the compound with a higher titer and/or purity compared to a cell expressing the first group of enzymes but no heterologous Ncb5or when cultivated in the same conditions, preferably wherein said cell is a yeast cell, such as an oleaginous yeast cell, or a plant cell.
2. The cell according to claim 1, wherein the first enzyme or group of enzymes comprises or consists of:
 - a) one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA, whereby the cell is capable of producing a desaturated fatty acyl-CoA with a higher titer and/or purity compared to a cell expressing said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions;
 - b) one or more fatty acyl reductase (FAR) capable of converting a fatty acyl-CoA to a fatty alcohol, whereby the cell is capable of producing a fatty alcohol with a higher titer and/or purity compared to a cell expressing said one or more FAR but no heterologous Ncb5or when cultivated in the same conditions; or
 - c) one or more FAR and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol, whereby the cell is capable of producing a desaturated fatty alcohol with a higher titer and/or purity compared to a cell expressing said one or more FAR and said one or more desaturase but no heterologous Ncb5or when cultivated in the same conditions.
3. The cell according to any one of the preceding claims, wherein the Ncb5or is native to a plant, an insect or a mammal, such as *Homo sapiens*, preferably wherein the Ncb5or is native to an insect, such as an insect of the genus

- 5 *Agrotis*, *Amyelois*, *Aphantopus*, *Arctia*, *Bicyclus*, *Bombus*, *Bombyx*, *Chilo*,
Cydia, *Danaus*, *Drosophila*, *Eumeta*, *Galleria*, *Helicoverpa*, *Heliothis*,
Hyposmocoma, *Leptidea*, *Lobesia*, *Manduca*, *Operophtera*, *Ostrinia*, *Papilio*,
Papilio, *Pieris*, *Plutella*, *Spodoptera*, *Trichoplusia* and *Vanessa*, such as
 wherein the Ncb5or is native to an insect selected from *Agrotis segetum*,
Amyelois transitella, *Aphantopus hyperantus*, *Arctia plantaginis*, *Bicyclus*
anyana, *Bombus terrestris*, *Bombyx mandarina*, *Bombyx mori*, *Chilo*
suppressalis, *Cydia pomonella*, *Danaus plexippus*, *Drosophila grimshawi*,
 10 *Drosophila melanogaster*, *Eumeta japonica*, *Galleria mellonella*, *Helicoverpa*
armigera, *Heliothis virescens*, *Hyposmocoma kahamanoa*, *Leptidea sinapis*,
Lobesia botrana, *Manduca sexta*, *Operophtera brumata*, *Ostrinia furnacalis*,
Papilio machaon, *Papilio polytes*, *Papilio xuthus*, *Pieris rapae*, *Plutella*
xylostella, *Spodoptera frugiperda*, *Spodoptera litura*, *Trichoplusia ni* and
Vanessa tameamea.
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4. The cell according to any one of the preceding claims, wherein the Ncb5or is
 selected from the group of Ncb5ors set forth in SEQ ID NOs: 111 to 114, SEQ
 ID NO: 124 and SEQ ID NOs: 182 to 185, or variants having at least 70%
 identity thereto, such as at least 75% identity, such as at least 80% identity,
 20 such as at least 85% identity, such as at least 90% identity, such as at least
 95% identity thereto.
5. The cell according to any one of the preceding claims, wherein the desaturase
 is native to a plant, such as *Ricinus communis* or *Pelargonium hortorum*, or an
 25 insect, such as of the *Diptera*, the *Coleoptera*, or the *Lepidoptera* order, such as
 of the genus *Agrotis*, *Antheraea*, *Argyrotaenia*, *Amyelois*, *Bombus*, *Bombyx*,
Cadra, *Chauliognathus*, *Chilo*, *Choristoneura*, *Cydia*, *Dendrophilus*, *Diatraea*,
Drosophila, *Ephesia*, *Epiphyas*, *Grapholita*, *Helicoverpa*, *Lampronia*, *Lobesia*,
Manduca, *Ostrinia*, *Pectinophora*, *Plodia*, *Plutella*, *Thalassiosira*,
 30 *Thaumetopoea*, *Tribolium*, *Trichoplusia*, *Spodoptera* or *Yponomeuta*, such as
Agrotis segetum, *Antheraea pernyi*, *Argyrotaenia velutiana*, *Amyelois transitella*,
Bombus lapidarius, *Bombyx mori*, *Cadra cautella*, *Chauliognathus lugubris*,
Chilo suppressalis, *Choristoneura parallela*, *Choristoneura rosaceana*, *Cydia*
pomonella, *Dendrophilus punctatus*, *Diatraea saccharalis*, *Drosophila*
 35 *ananassae*, *Drosophila melanogaster*, *Drosophila virilis*, *Drosophila yakuba*,

- 5 *Ephestia elutella*, *Ephestia kuehniella*, *Epiphyas postvittana*, *Grapholita molesta*, *Helicoverpa assulta*, *Helicoverpa zea*, *Lampronia capitella*, *Lobesia botrana*, *Manducta sexta*, *Ostrinia furnacalis*, *Ostrinia nubilalis*, *Pectinophora gossypiella*, *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*,
Spodoptera littoralis, *Spodoptera litura*, *Thalassiosira pseudonana*,
Thaumetopoea pityocampa, *Tribolium castaneum*, *Trichoplusia ni* or
Yponomeuta padella .
- 10 6. The cell according to any one of the preceding claims, wherein the desaturase is selected from the group consisting of a $\Delta 3$ desaturase, a $\Delta 5$ desaturase, a $\Delta 6$ desaturase, a $\Delta 7$ desaturase, a $\Delta 8$ desaturase, a $\Delta 9$ desaturase, a $\Delta 10$ desaturase, a $\Delta 11$ desaturase, a $\Delta 12$ desaturase, a $\Delta 13$ desaturase and a $\Delta 14$ desaturase, preferably wherein the desaturase is a $\Delta 9$ desaturase or a $\Delta 11$ desaturase, and/or wherein the desaturase is selected from the group of
15 desaturases set forth in SEQ ID NOs: 1 to 38 and SEQ ID NOs: 126 to 139, or variants having at least 70% identity thereto, such as at least 75% identity, such as at least 80% identity, such as at least 85% identity, such as at least 90% identity, such as at least 95% identity.
- 20 7. The cell according to any one of the preceding claims, wherein the FAR is native to an insect such as an insect of the *Lepidoptera* order, such as of the genus *Agrotis*, *Amyelois*, *Bicyclus*, *Bombus*, *Chilo*, *Chrysodeixis*, *Cydia*, *Helicoverpa*, *Heliothis*, *Manducta*, *Ostrinia*, *Plodia*, *Plutella*, *Spodoptera*, *Trichoplusia*, *Tyta* or *Yponomeuta*, or wherein the FAR is native to a bacteria,
25 such as of the genus *Marinobacter*, preferably wherein the FAR is a fatty acyl reductase native to *Agrotis segetum*, *Amyelois transitella*, *Bicyclus anynana*, *Bombus lapidaries*, *Chilo suppressalis*, *Chrysodeixis includes*, *Cydia pomonella*, *Helicoverpa armigera*, *Helicoverpa assulta*, *Heliothis virescens*, *Heliothis subflexa*, *Manducta sexta*, *Marinobacter algicola*, *Ostrinia furnacalis*,
30 *Plodia interpunctella*, *Plutella xylostella*, *Spodoptera exigua*, *Spodoptera frugiperda*, *Spodoptera littoralis*, *Spodoptera litura*, *Trichoplusia ni*, *Tyta alba* or *Yponomeuta rorellus*, or a functional variant thereof having at least 80% identity thereto.

8. The cell according to any one of the preceding claims, wherein the FAR is selected from the group of FARs set forth in SEQ ID NOs: 77 to 93 and SEQ ID NOs: 154 to 167, or variants having at least 70% identity thereto, such as at least 75% identity, such as at least 80% identity, such as at least 85% identity, such as at least 90% identity, such as at least 95% identity.
9. A method for increasing the activity of at least one enzyme selected from the group consisting of desaturases and fatty acyl CoA reductases (FARs), said method comprising the steps of:
- providing a desaturase capable of introducing at least one double bond in a fatty acyl-CoA, thereby converting at least part of said fatty acyl-CoA to a desaturated fatty-acyl-CoA; and/or
 - providing a FAR capable of converting at least part of said desaturated fatty acyl-CoA to a desaturated fatty alcohol, thereby producing said desaturated fatty alcohol; and
 - contacting said desaturase and/or FAR with an Ncb5or, thereby increasing the activity of said desaturase and/or FAR compared to the activity of said desaturase and/or FAR in the absence of said Ncb5or, wherein the activity is measured under the same conditions;
- wherein the increase in activity is measured by measuring the concentration and/or purity of product formed by the desaturase and/or the FAR, preferably wherein said cell is a cell according to any one of the preceding claims.
10. A method for production of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA in a cell, said method comprising the steps of:
- providing a cell and incubating said cell in a medium; and
 - expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
 - expressing in said cell an Ncb5or;
 - optionally, recovering said compound,
- preferably wherein said cell is a cell according to any one of claims 1 to 8.

11. A method for increasing the titer and/or purity of a compound selected from a desaturated fatty alcohol, a saturated fatty alcohol, a desaturated fatty alcohol acetate, and a desaturated fatty acyl-CoA produced in a cell capable of synthesising one or more fatty acyl-CoAs and/or capable of importing fatty acyl-CoAs from its environment, said method comprising the steps of:
- expressing in said cell a first enzyme or group of enzymes capable of converting a fatty acyl-CoA to said compound, thereby converting at least part of said fatty acyl-CoA to said compound; and
 - expressing in said cell an Ncb5or, thereby increasing the titer and/or purity of said compound compared to the titer and/or purity from a cell not expressing said Ncb5or in the same conditions;
 - optionally, recovering said compound, preferably wherein said cell is a cell according to any one of claims 1 to 8.
12. The method according to claim 11, wherein the first enzyme or group of enzymes consists of:
- one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty acyl-CoA and wherein said compound is a desaturated fatty acyl-CoA;
 - one or more FAR capable of converting a fatty acyl-CoA to a saturated fatty alcohol and wherein said compound is a saturated fatty alcohol; or
 - one or more FAR and one or more desaturase capable of converting a fatty acyl-CoA to a desaturated fatty alcohol and wherein said compound is a desaturated fatty alcohol;
- and/or wherein the titer and/or purity of desaturated fatty alcohols and/or fatty alcohol acetates, the titer and/or purity of saturated fatty alcohols and/or fatty alcohol acetates and/or the total titer of saturated fatty alcohols and/or fatty alcohol acetates is increased at least 3% compared to the titer and/or purity from a cell not expressing said Ncb5or, such as at least 4%, such as at least 5%, such as at least 10%, such as at least 15%, such as at least 20%, such as at least 25%, such as at least 30%, such as at least 35%, such as at least 40%, such as at least 45%, such as at least 50%, such as at least 55%, such as at least 60%, such as at least 70%, such as at least 80%, such as at least 90%, such as at

least 100%, such as at least 150%, such as at least 200%, such as at least 250%.

- 5 13. A system of nucleic acid constructs comprising nucleic acids encoding an Ncb5or and:
- a. a desaturase capable of introducing at least one double bond in a fatty acyl-CoA; and/or
 - b. a fatty acyl-CoA reductase capable of converting at least part of a desaturated fatty acyl-CoA to a desaturated fatty alcohol.
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- 15 14. Use of an Ncb5or in a method for increasing the activity of one or more enzymes, preferably wherein the one or more enzymes is one or more membrane-bound enzymes, and/or wherein the one or more enzymes is selected from the group consisting of desaturases and fatty acyl reductases, optionally wherein the increase in activity of said one or more enzymes is at least 1.2-fold for the desaturase and/or the FAR, such as at least 1.3-fold, such as at least 1.4-fold, such as at least 1.5-fold, such as at least 1.6-fold, such as at least 1.7-fold, such as at least 1.8-fold, such as at least 1.9-fold, such as at least 2-fold, such as at least 3-fold, such as at least 4-fold, such as at least 5-fold, such as at least 6-fold, such as at least 7-fold, such as at least 8-fold, such as at least 9-fold, such as at least 10-fold, such as at least 15-fold, such as at least 20-fold, such as at least 30-fold, such as at least 40-fold, such as at least 50-fold; wherein the increase in activity of said one or more enzymes is compared to the activity of said one or more enzymes in the absence of said
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- 25 Ncb5or, wherein the activity is measured under the same conditions, wherein the increase is measured by measuring the concentration of product formed by the one or more enzymes.
- 30 15. A method of monitoring the presence of pest or disrupting the mating of pest, said method comprising the steps of:
- a. producing a desaturated fatty alcohol and optionally a desaturated fatty alcohol acetate and/or a desaturated fatty aldehyde according to the method of any one of claims 9 to 12; and

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- b. formulating said desaturated fatty alcohol and optionally said desaturated fatty alcohol acetate and/or said desaturated fatty aldehyde as a pheromone composition; and
 - c. employing said pheromone composition as an integrated pest management composition.