CLAIMS

1. A genetically modified plant or part thereof comprising a polynucleotide encoding an acyl activating enzyme 1 (AAE1), a polynucleotide encoding an olivetol synthase (OLS) and a polynucleotide encoding an olivetolic acid cyclase (OAC), optionally further comprising a polynucleotide encoding a plastid localised prenyltransferase polypeptide, preferably cannabigerolic acid synthase (CBGAS),
wherein each polynucleotide is operably linked to a promoter which is capable of directing expression of the polynucleotide in the plant or part thereof,
wherein the polynucleotides are codon optimised for expression in the plant or part thereof, and
when expressed in the plant or part thereof in the presence of hexanoic acid (C6) and geranyl-pyrophosphate (GPP), the polypeptides encoded by the polynucleotides increase the production of cannabigerolic acid (CBGA) when compared to a wild-type plant or part thereof.

2. The genetically modified plant or part thereof of claim 1, wherein
i) the polynucleotides are comprised within a vector, preferably a viral vector,
wherein the polynucleotides encode a fusion polypeptide comprising a plastid transporting peptide; and/or,
wherein the polypeptide encoded by the polynucleotides are expressed in the presence of a plastid localised prenyltransferase; and/or
ii) when expressed in the plant or part thereof in the presence of hexanoic acid (C6) and geranyl-pyrophosphate (GPP), the polypeptides encoded by the polynucleotides increase the production of cannabigerolic acid (CBGA) compared to a wild-type plant or part thereof.

3. The plant or part thereof of claim 1 or 2, wherein the genetically modified plant or part thereof is a high biomass plant, preferably selected from the group consisting of *Acrocomia aculeata* (macauba palm), *Arabidopsis thaliana, Aracinis hypogaea* (peanut), *Astrocaryum murumuru (*murumuru), *Astrocaryum vulgare* (tucuma), *Attalea geraensis* (Indaia-rateiro), *Attalea humilis* (American oil palm), *Attalea oleifera* (andaia), *Attalea phalerata* (uricuri), *Attalea speciosa* (babassu), *Avena sativa* (oats), *Beta vulgaris* (sugar beet), *Brassica sp.* such as *Brassica carinata, Brassica juncea, Brassica napobrassica, Brassica napus (canola),*

Camelina sativa (false flax), *Cannabis sativa* (hemp), *Carthamus tinctorius* (safflower), *Caryocar brasiliense* (pequi), *Cocos nucifera* (Coconut), *Crambe abyssinica (Abyssinian kale), Cucumis melo* (melon), *Elaeis guineensis* (African palm), *Glycine max* (soybean), *Gossypium hirsutum* (cotton), *Helianthus sp.* such as *Helianthus annuus* (sunflower), *Hordeum vulgare* (barley), *Jatropha curcas* (physic nut), *Joannesia princeps* (arara nut-tree), *Lemna sp.* (duckweed) such as *Lemna aequinoctialis, Lemna disperma, Lemna ecuadoriensis, Lemna gibba* (swollen duckweed), *Lemna japonica, Lemna minor, Lemna minuta, Lemna obscura, Lemna paucicostata, Lemna perpusilla, Lemna tenera, Lemna trisulca, Lemna turionifera, Lemna valdiviana, Lemna yungensis, Licania rigida* (oiticica), *Linum usitatissimum* (flax), *Lupinus angustifolius* (lupin), *Mauritia flexuosa* (buriti palm), *Maximiliana maripa* (inaja palm), *Miscanthus sp.* such as *Miscanthus x giganteus* and *Miscanthus sinensis, Nicotiana sp.* (tobacco) such as *Nicotiana tabacum, Nicotiana benthamiana, Nicotiana sylvestris, Nicotiana glauca, Nicotiana rustica, Nicotiana glutinosa, Nicotiana suaveolens, or Nicotiana landsdorffii, Oenocarpus bacaba* (bacaba- do-azeite), *Oenocarpus bataua* (pataua), *Oenocarpus distichus* (bacaba-de-leque), *Oryza sp.* (rice) such as *Oryza sativa* and *Oryza glaberrima, Panicum virgatum* (switchgrass), *Paraqueiba paraensis* (mari), *Persea amencana* (avocado), *Pongamia pinnata* (Indian beech), *Populus trichocarpa, Ricinus communis* (castor), *Saccharum sp.* (sugarcane), *Sesamum indicum* (sesame), *Solanum tuberosum* (potato), *Sorghum sp.* such as *Sorghum bicolor, Sorghum vulgare, Theobroma grandiforum* (cupuassu), *Trifolium sp., Trithrinax brasiliensis* (Brazilian needle palm)*, Triticum sp.* (wheat) such as *Triticum aestivum* and *Zea mays* (corn).

4. The plant or part thereof of claims 1 to 3, wherein the plant is *Nicotiana sp.,* preferably *Nicotiana benthamiana* or *Nicotiana tabacum.*

5. The plant or part thereof of any one of claims 1 to 4, wherein
i) at least one polypeptide is active in the cytosol of the plant or part thereof; and/or
ii) one or more polynucleotides, optionally each polynucleotide, encode a fusion polypeptide comprising a plastid transporting peptide, preferably a chloroplast transit peptide (CTP).

6. The plant or part thereof of any one of claims 1 to 5, wherein the plant or part thereof further comprises at least one polynucleotide selected from the group consisting of a polynucleotide encoding an acyl-lipid thioesterase, optionally

wherein the polynucleotide encodes a fusion polypeptide comprising a plastid transporting peptide.

7. The plant or part thereof of any one of claims 1 to 6, wherein the plant or part thereof further comprises at least one polynucleotide selected from a polynucleotide encoding a plastid lipase 1 (PLIP1) and a polynucleotide encoding a tomato 13-lipoxygenase (TomLoxC), optionally wherein the polynucleotide encodes a fusion polypeptide comprising a plastid transporting peptide.

8. A nucleic acid construct encoding polypeptides for expression in a plant or part thereof, comprising one or more polynucleotides encoding an acyl activating enzyme 1 (AAE1), a polynucleotide encoding an olivetol synthase (OLS), and a polynucleotide encoding an olivetolic acid cyclase (OAC), optionally further encoding one or more of: a plastid transporting peptide, a prenyltransferase, a plastid acyl-lipid thioesterase, a plastid lipase, and a plastid tomato 13-lipoxygenase;
wherein the polynucleotide is operably linked to a promoter which is capable of directing expression of the one or more or all polynucleotides in the plant or part thereof,
optionally, wherein the one or more or all polynucleotides are operably linked to a polynucleotide encoding a plastid transporting peptide;
optionally, wherein the nucleic acid construct encodes a fusion polypeptide comprising the plastid transporting peptide, and
when expressed, the polypeptide encoded by the polynucleotide/s increase the production of cannabigerolic acid (CBGA) compared to a wild-type plant or part thereof.

9. The nucleic acid construct of claim 8, further comprising one or more of the following features:
i) a polynucleotide encoding a silencing suppressor polypeptide, preferably a p19 silencing suppressor polypeptide;
ii) the nucleic acid construct is comprised within a vector suitable for expression in a plant or part thereof;
iii) one or more or all polynucleotides are operably linked to a promoter which is capable of directing expression of the polypeptide encoded by the polynucleotide in a plant or part thereof;

iv) the one or more or all polynucleotides are operably linked to a polynucleotide encoding a plastid transporting peptide;

v) the nucleic acid construct encodes a fusion polypeptide comprising a plastid transporting peptide;

vi) the acyl-lipid thioesterase is ALT4;

vii) the plastid lipase is plastid lipase 1 (PLIP1);

viii) production of CBGA is increased by at least about 1.5-about 2 fold, about 2-about 2.5 fold, about 2.5-about 3.0 fold, about 3-about 3.5 fold, about 3.5-about 4.0 fold, about 4-about 4.5 fold, about 4.5-about 5.0 fold or about 5-about 5.5 fold or more when expressed in a plant or part thereof, compared to a wild-type plant or part thereof; and

ix) production of CBGA is increased at least about 10%–about 20%, about 20%–about 30%, about 30%–about 40%, about 40%–about 50%, about 50%–about 60%, about 60%–70%, about 70%–about 80%, about 80%–about 90%, about 90%–about 100%, about 100%–about 120%, about 120%–about 140%, about 140%–about 160%, about 160%–about 180%, about 180%–about 200%, about 200%–about 220%, about 220%–about 240%, about 240%–about 260%, about 260%–about 280%, about 280%–about 300%, about 300%–about 320%, about 320%–about 340%, about 340%–about 360%, about 360%–about 380%, about 400%–about 420% or more when expressed in a plant or part thereof, compared to a wild–type plant or part thereof.

10. A fusion polypeptide for expression in a plant or part thereof, comprising:

i) a polypeptide selected from the group consisting of a polyketide synthase, a polyketide cyclase, an acyl-activating enzyme, a prenyltransferase, a plastid acyl-lipid thioesterase, a plastid lipase or a plastid tomato 13-lipoxygenase, and

ii) a plastid transporting sequence,

wherein the polypeptide of (i) increases the production of cannabigerolic acid (CBGA) in the presence of hexanoic acid (C6) and geranyl-pyrophosphate (GPP), when compared to a wild type plant or part thereof, optionally wherein the plastid transporting sequence is a chloroplast transit peptide (CTP).

11. The nucleic acid construct of claim 8 or 9, or the fusion polypeptide of claim 10, wherein the polyketide synthase is olivetol synthase (OLS), the polyketide cyclase is olivetolic acid cyclase (OAC), the acyl-activating enzyme is acyl

activating enzyme 1 (AAE1), the plastid acyl-lipid thioesterase is ALT4, the plastid lipase is PLIP1, the plastid tomato 13-lipoxygenase is TomLoxC and the prenyltransferase is cannabigerolic acid synthase (CBGAS), preferably wherein plastid transporting peptide is a chloroplast transit peptide (CTP).

12. The plant or part thereof of any one of claims 1 to 7, or the nucleic acid construct of any one of claims 8, 9, or 11 or the fusion polypeptide of claim 10 or 11, wherein one or more apply:

i) the polynucleotide encoding AAE1 comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5% at least 99.8% or identical to a sequence set forth as any one of SEQ ID NO:5, SEQ ID NO:6 and SEQ ID NO:7;

ii) the polynucleotide encoding OLS comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to a sequence set forth as any one of SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:10;

iii) the polynucleotide encoding OAC comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to a sequence set forth as any one of SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13;

iv) the polynucleotide encoding the plastid transporting peptide comprises a sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to the sequence set forth as SEQ ID NO:15; and

v) the polynucleotide encoding a prenyltransferase comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to a sequence set forth as SEQ ID NO:14.

13. The plant or part thereof of claim 6, or the nucleic acid construct of any one of claims 8, 9 or 11 or the fusion polypeptide of claim 10 or 11, wherein one or more of the following features:

i) the polynucleotide encoding the acyl-lipid thioesterase comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to a sequence set forth as SEQ ID NO:24 or 25;

ii) the polynucleotide encoding PLIP1 comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to the sequence set forth as SEQ ID NO:26; and

iii) the polynucleotide encoding TomLoxC comprises a nucleotide sequence which is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, at least 99.8% or identical to the sequence set forth as SEQ ID NO:27.

14. A method of producing a cannabinoid in a plant or plant part thereof, the method comprising:

i) obtaining a plant or part thereof comprising the nucleic acid construct of claims 8 or 9 or 11 to 13 cultivated under conditions sufficient for expression of the polypeptide in the plant or plant part, wherein when expressed in the presence of hexanoic acid (C6) and geranyl-pyrophosphate (GPP), the polypeptide increases the production of cannabigerolic acid (CBGA) in the plant or plant part when compared to a wild type plant or plant part;

ii) recovering the CBGA produced at i); and

iii) optionally feeding the CBGA to a genetically modified microorganism, preferably yeast or bacteria; and

iv) chemically, physically, or biochemically converting the CBGA, optionally by (a) using the CBGA as a feedstock; or optionally by (b) CBGA decarboxylation, preferably by incubation of CBGA with heat or light;

thereby producing the cannabinoid.

15. A genetically modified and/or recombinant plant cell for producing cannabigerolic acid (CBGA) comprising the nucleic acid construct of any one of claims 8 or 9 or 11 to 13.

16. A process for identifying a polynucleotide encoding a polypeptide for producing cannabigerolic acid (CBGA) in a plant, or part thereof, or plastid thereof, or cell thereof, the process comprising:

i) obtaining the nucleic acid construct of any one of claims 8 or 9 or 11 to 13;

ii) introducing the nucleic acid construct into a plant, part thereof, or plastid or cell thereof;

iii) determining whether the level of CBGA is increased relative to a corresponding wild-type plant, part thereof or plastid or cell thereof lacking the nucleic acid construct; and

iv) optionally, selecting a polynucleotide, which when expressed produces a polypeptide for producing CBGA.

17. A process for producing an industrial product, the process comprising the steps of:

i) obtaining a plant or part thereof of any one of claims 1 to 7, or 12, or 14;

ii) processing the plant or part thereof;

iii) converting at least some of a cannabinoid in the plant or part thereof of step i), or in the processed plant, part thereof, or plastid, obtained by step ii), by applying heat, chemical, or enzymatic means, or any combination thereof, to generate a cannabinoid *in situ*; and

iv) recovering the cannabinoid;

thereby producing the industrial product.

18. A process for producing extracted cannabigerolic acid (CBGA), the process comprising the steps of:

i) obtaining a plant or part thereof of any one of claims 1 to 7, or 12, or 14;

ii) extracting CBGA from the plant or part thereof; and

iii) recovering the extracted CBGA, thereby producing extracted CBGA.

19. A process of producing a cannabigerolic acid (CBGA) enriched extract, the process comprising the steps of:

i) obtaining a plant or part thereof of any one of claims 1 to 7, or 12, or 14;

ii) processing the plant or part thereof of step i);

iii) centrifuging the processed plant or part thereof from step ii) to obtain extracts;

iv) filtering the extract obtained by step iii);

v) drying the filtered extract of step iv) and resuspending in buffer solution;

vi) purifying the extract of step v) using a solid-phase extraction column; and

vii) recovering the CBGA enriched extract, thereby producing the CBGA enriched extract.

20. A method for producing a pharmaceutical composition comprising:

i) obtaining the extract produced by the process of claim 18 or 19, or the cannabinoid produced by the method of claim 14 or the process of claim 17; and

ii) formulating the extract or cannabinoid with one or more pharmaceutically acceptable carriers;

thereby producing a pharmaceutical composition.

21. Use of a therapeutically effective amount of the cannabinoid obtained by the method of claim 14, or the process of claim 17, the extract obtained by the process of claims 18 or 19, or the pharmaceutical composition obtained by method of claim 20 in the manufacture of a medicament for treating a condition or disease responsive to cannabinoid treatment.