CLAIMS:

~~1. A variant of a LovD polypeptide shown in SEQ ID NO:1, the variant LovD polypeptide comprising an amino acid substitutions at amino acid residue position: G275.~~

~~2. The variant LovD polypeptide of claim 1, wherein:~~

~~the amino acid substitution comprises any one of the 19 amino acids not found at the amino acid residue position on the LovD polypeptide shown in SEQ ID NO:1; and~~

~~the variant further comprises amino substitutions at amino acid residue positions K26 and/or L361.~~

~~3. The variant LovD polypeptide of claim 1 or 2, wherein the variant LovD polypeptide comprises amino acid substitution: G275S.~~

1.~~4.~~ ~~The~~ A variant of a LovD polypeptide shown in SEQ ID NO:1, ~~of claim 1 or 2, wherein~~ the variant LovD polypeptide ~~comprises~~ consisting of amino acid substitutions at:

~~;~~

amino acid residue positions C40; C60; D12; A86; and G275;

amino acid residue positions C40; C60; D12; A86; C40; C60; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; C40; C60; H161; A190; and G275;

amino acid residue positions C40; C60; D12; A86; A190; and G275;

amino acid residue positions C40; C60; A10; D12; K26; A86; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; G275; V334 and L361; or

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; G275; and V334.

~~5.~~2. ~~The~~ A variant of a LovD polypeptide shown in SEQ ID NO:1, ~~of claim 1 or 2, wherein~~ the variant LovD polypeptide ~~comprises~~ consisting of amino acid substitutions:

D12G, C40A, C60N, A86V, A190T and G275S;

D12G, K26E, C40A, C60N, A86V, H161Y, A190T and G275S; or

D12G, K26E, C40A, C60N, A86V, H161Y, A190T; G275S and V334F.

~~6.~~3. The variant LovD polypeptide of claim~~s 1-5~~ 1 or 2, wherein the variant exhibits:

a decreased aggregation;

an improved thermal stability;

an improved catalytic activity;

an improved k_{cat}/K_m value;

an improved soluble expression level; and/or

an improved whole cell activity at 25°C

as compared to the LovD polypeptide shown in SEQ ID NO:1.

~~7.~~4. An isolated polynucleotide ~~having at least a 95% sequence identity to a polynucleotide~~ encoding a variant LovD polypeptide of any one of claims ~~1-6~~1-3.

~~8.~~5. A vector comprising the polynucleotide of claim ~~7~~4.

~~9.~~6. The vector of claim ~~8~~ 5 operably linked to control sequences recognized by a host cell transformed with the vector.

~~10.~~7. A host cell comprising the vector of claim ~~9~~6.

~~11.~~8. The host cell of claim ~~10~~ 7 wherein the host cell is an *Escherichia coli, Aspergillus terreus, Monascus ruber, Monascus purpureus, Monascus pilosus, Monascus vitreus, Monascus pubigerus, Candida cariosilognicola, Aspergillus oryzea, Doratomyces stemonitis, Paecilomyces virioti, Penicillum citrinum, Penicillin chrysogenum, Scopulariopsis brevicaulis or Trichoderma viride.*

~~12.~~9. A process for producing a variant LovD polypeptide comprising culturing the host cell of claim ~~11~~ 8 under conditions suitable for expression of a polypeptide encoded by a polynucleotide of claim ~~6~~ 3 so that the variant LovD polypeptide is produced.

~~13.~~10. A chimeric molecule comprising a variant LovD polypeptide of any one of claims ~~1-6~~1-3, fused to a heterologous amino acid sequence.

~~14.~~11. A monoclonal antibody which specifically binds to a variant LovD polypeptide of any one of claims ~~1-6~~1-3.

~~15.~~12. A method of making a variant of a LovD polypeptide shown in SEQ ID NO:1 comprising:

using a polynucleotide mutagenesis procedure to generate a population of mutants of the LovD polynucleotide shown in SEQ ID NO: 5; and

expressing a population of LovD polypeptide variants encoded by the population of LovD polynucleotide mutants;

so that a variant of a LovD polypeptide shown in SEQ ID NO:1 is made, wherein the polynucleotide mutagenesis procedure is controlled so as to generate a substitution mutation at a codon that encodes amino acid residue position: G275.

~~16.~~13. The method of claim ~~15~~12, wherein the polynucleotide mutagenesis procedure is a saturation mutagenesis or an error prone polymerase chain reaction procedure.

~~17.~~14. The method of claim ~~15~~12, further comprising screening one or more members of the population of LovD polypeptide variants so as to identify a variant that exhibits: a decreased aggregation; an improved thermal stability; an improved acyltransferase activity; an improved kcat/Km value; an improved soluble expression level; and/or an improved whole cell activity at 25°C, as compared to the LovD polypeptide shown in SEQ ID NO:1.

~~18.~~15. The method of claim ~~15~~12, wherein the polynucleotide mutagenesis procedure is controlled so as to generate a substitution mutation at a codon that encodes amino acid residue position: K26; and/or L361.

~~19.~~16. A method of making simvastatin comprising the steps of:

(1) combining together monacolin J; an acyl thioester that donates an acyl moiety to the C8 hydroxyl group of monacolin J in the presence of LovD acyltransferase; and a variant of a LovD acyltransferase polypeptide shown in SEQ ID NO:1, the variant LovD polypeptide comprising

an amino acid substitution at: ~~amino acid residue position G275~~

amino acid residue positions C40; C60; D12; A86; and G275;

amino acid residue positions C40; C60; D12; A86; C40; C60; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; C40; C60; H161; A190; and G275;

amino acid residue positions C40; C60; D12; A86; A190; and G275;

amino acid residue positions C40; C60; A10; D12; K26; A86; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; and G275;

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; G275; V334 and L361; or

amino acid residue positions C40; C60; D12; K26; A86; H161; A190; G275; and V334; and

(2) allowing the variant LovD polypeptide to use an acyl group from the acyl thioester to regioselectively acylate the C8 hydroxyl group of monacolin J;

so that simvastatin is made.

~~20.~~17. The method of claim ~~19~~16, wherein the monacolin J; the acyl thioester and the variant LovD polypeptide are combined in a fermentation media in the presence of an isolated organism that produces the LovD acyltransferase wherein the isolated organism is at least one of:

(a) *Aspergillus terreus*;

(b) *Aspergillus terreus* that does not express LovF polypeptide of SEQ ID NO: 3;

(c) *Escherichia coli*; or

(d) *Escherichia coli* that does not express *bio*H polypeptide of SEQ ID NO: 4.

~~21.~~18. The method of claim ~~19~~16, wherein the acyl thioester is selected to possess at least one of the following properties:

(a) is a butyrlyl-thioester, a N-acetylcysteamine thioester or a methyl-thioglycolate thioester;

(b) comprises medium chain length (C3-C6) acyl group moieties;

(c) is able to cross the cellular membranes of *Escherichia coli* or *Aspergillus terreus* cells growing within a fermentation media; or

(d) is selected from the group consisting of α-dimethylbutyryl-S-methyl-mercaptopropionate (DMB-S-MMP), dimethylbutyryl-S-ethyl mercaptopropionate (DMB-S-EMP) and dimethylbutyryl-S-methyl thioglycolate (DMB-S-MTG) and dimethylbutyryl-S-methyl mercaptobutyrate (DMB-S-MMB).

~~22.~~19. The method of claim ~~21~~18, wherein the acyl thioester is α-dimethylbutyryl-S-methyl-mercaptopropionate, and wherein the α-dimethylbutyryl-S-methyl-mercaptopropionate is present in the fermentation media in a concentration range of 1mM-100mM.

~~23.~~20. The method of claim ~~20~~17, wherein the monacolin J is produced by an isolated organism within the fermentation media.

~~24.~~21. The method of claim ~~20~~17, wherein the isolated organism is grown under at least one of the following conditions:

(a) at a temperature between 25-40°C;

(b) for a time period between at least 4 to at least 48 hours;

(c) at a pH between 7-8; or

(d) in a fermentation media comprising LB, F1 or TB media.

~~25.~~22. The method of claim ~~19~~16, further comprising purifying the simvastatin made by the method by at least one purification step comprising:

(a) lysis of cells of an isolated organism present in the combination;

(b) centrifugation;

(c) precipitation of a free acid form of simvastatin;

(d) conversion of a free acid form of simvastatin to a simvastatin salt;

(e) filtration; or

(f) high performance liquid chromatography (HPLC).

~~26.~~23. The method of claim ~~19~~16, wherein the method:

(a) produces a composition of matter comprising 0%-1% of the monacolin J that was initially combined with the acyl thioester that donates an acyl moiety to the C8 hydroxyl group of monacolin J in the presence of LovD acyltransferase; and/or

(b) results in at least 95% of the monacolin J added to the combination being converted to simvastatin.

~~27.~~24. The method of claim ~~19~~16, wherein the variant LovD polypeptide comprises amino acid substitutions:

D12G, C40A, C60N, A86V, A190T and G275S;

D12G, K26E, C40A, C60N, A86V, H161Y, A190T and G275S; or

D12G, K26E, C40A, C60N, A86V, H161Y, A190T; G275S and V334F.

~~28.~~25. The method of claim ~~19~~16, wherein the variant LovD polypeptide exhibits:

a decreased aggregation;

an improved thermal stability;

an improved catalytic activity;

an improved k_{cat}/K_m value;

an improved soluble expression level; and/or

an improved whole cell activity at 25°C

as compared to the LovD polypeptide shown in SEQ ID NO:1.

~~29.~~26. A composition of matter comprising:

monacolin J;

an acyl thioester that donates an acyl moiety to the C8 hydroxyl group of monacolin J in the presence LovD acyltransferase;

a variant of a LovD acyltransferase polypeptide shown in SEQ ID NO:1, the variant LovD polypeptide comprising an amino acid substitution at amino acid residue position G275; and

simvastatin.

~~30.~~27. A composition of matter comprising:

hydrolyzed pravastatin tetra-ol;

an acyl thioester that donates an acyl moiety to the C8 hydroxyl group of hydrolyzed pravastatin tetra-ol in the presence LovD acyltransferase;

a variant of a LovD acyltransferase polypeptide shown in SEQ ID NO:1, the variant LovD polypeptide comprising an amino acid substitution at amino acid residue position: G275; and

huvastatin.

~~31.~~28. A method of making huvastatin comprising the steps of:

(1) combining together hydrolyzed pravastatin tetra-ol; an acyl thioester that donates an acyl moiety to the C8 hydroxyl group of hydrolyzed pravastatin tetra-ol in the presence of LovD acyltransferase; and a variant of a LovD acyltransferase polypeptide shown in SEQ ID NO:1, the variant LovD polypeptide comprising an amino acid substitution at amino acid residue position G275; and

(2) allowing the variant LovD polypeptide to use an acyl group from the acyl thioester to regioselectively acylate the C8 hydroxyl group of hydrolyzed pravastatin tetra-ol;

so that huvastatin is made.

~~32.~~29. The method of claim ~~31~~28, wherein the variant LovD polypeptide comprises amino acid substitutions:

D12G, C40A, C60N, A86V, A190T and G275S;

D12G, K26E, C40A, C60N, A86V, H161Y, A190T and G275S; or

D12G, K26E, C40A, C60N, A86V, H161Y, A190T; G275S and V334F.

~~33.~~30. The method of claim ~~31~~28, wherein the acyl thioester is selected to possess at least one of the following properties:

(a) is a butyrlyl-thioester, a N-acetylcysteamine thioester or a methyl-thioglycolate thioester;

(b) comprises medium chain length (C3-C6) acyl group moieties;

(c) is able to cross the cellular membranes of *Escherichia coli* or *Aspergillus terreus* cells growing within a fermentation media; or

(d) is selected from the group consisting of α-dimethylbutyryl-S-methyl-mercaptopropionate (DMB-S-MMP), dimethylbutyryl-S-ethyl mercaptopropionate (DMB-S-EMP) and dimethylbutyryl-S-methyl thioglycolate (DMB-S-MTG) and dimethylbutyryl-S-methyl mercaptobutyrate (DMB-S-MMB).