WHAT IS CLAIMED:

1. A method for integrating a plurality of exogenous nucleic acids into a host cell genome, the method comprising:

(a) contacting a host cell with:

(i) a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid $(ES)_x$ comprises a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a target site $(TS)_x$ of said host cell genome; and

(ii) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$;

and

(b) recovering a host cell wherein each selected exogenous nucleic acid $(ES)_x$ has integrated at each selected target sequence $(TS)_x$,

wherein x is any integer from 1 to n wherein n is at least 2.

2. The method of claim 1, wherein $(HR1)_x$ is homologous to a 5' region of $(TS)_x$, and $(HR2)_x$, is homologous to a 3' region of $(TS)_x$.

3. The method of claim 1, wherein $(N)_x$ is capable of cleaving at a region positioned between said 5' and 3' regions of $(TS)_x$.

4. The method of claim 1, wherein a single nuclease is capable of cleaving each $(TS)_x$.

5. The method of claim 1, wherein n= 3, 4, 5, 6, 7, 8, 9 or 10.

6. The method of claim 1, wherein said recovering does not require integration of a selectable marker.

7. The method of claim 1, wherein said recovering occurs at a higher frequency as compared to not contacting the host cell with a nuclease capable of cleaving at said target site.

8. The method of claim 1, wherein said recovering occurs at a frequency of about one every 10, 9, 8, 7, 6, 5, 4, 3, or 2 contacted host cells, or clonal populations thereof, screened.

9. The method of claim 1, wherein said recovering comprises identifying said integrations by at least one method selected from the group consisting of PCR, Southern blot, restriction mapping, and DNA sequencing.

10. The method of claim 1, wherein $(N)_x$ is capable of cleaving an endogenous genomic sequence within $(TS)_x$.

11. The method of claim 1, wherein $(N)_x$ is capable of cleaving an exogenous sequence within $(TS)_x$.

12. The method of claim 11, wherein the exogenous sequence is a recognition sequence for a homing endonuclease.

13. The method of claim 12, wherein the homing endonuclease is F-cphI.

14. The method of claim 1, wherein $(ES)_x$ further comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$.

15. The method of claim 14, wherein $(D)_x$ is selected from the group consisting of a selectable marker, a promoter, a nucleic acid sequence encoding an epitope tag, a gene of interest, a reporter gene, and a nucleic acid sequence encoding a termination codon.

16. The method of claim 1, wherein $(ES)_x$ is linear.

17. The method of claim 1, wherein the host cell comprises one or more heterologous nucleotide sequences encoding one or more enzymes of a biosynthetic pathway.

18. The method of claim 17, wherein the one or more heterologous nucleotide sequences encoding one or more enzymes of a biosynthetic pathway are genomically integrated.

19. The method of claim 1, wherein each said exogenous nucleic acid $(ES)_x$ comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$, encoding an enzyme of a biosynthetic pathway.

20. The method of claim 19, wherein $(D)_x$ is a member of a library $(L)_x$ comprising a plurality of nucleic acid molecules that encode variants of an enzyme of a biosynthetic pathway.

21. The method of claim 1, wherein the host cell comprises one or more heterologous nucleotide sequences encoding one or more enzymes of a mevalonate (MEV) pathway for making isopentenyl pyrophosphate.

22. The method of claim 21, wherein the one or more enzymes of the mevaloante pathway are selected from acetyl-CoA thiolase, HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase and mevalonate pyrophosphate decarboxylase.

23. The method of claim 21, wherein the host cell comprises a plurality of heterologous nucleic acids encoding each the enzymes of a MEV pathway.

24. The method of claim 21, wherein each said exogenous nucleic acid $(ES)_x$ comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$, encoding a terpene synthase.

25. The method of claim 24, wherein the terpene synthase is selected from the group consisting of a monoterpene synthase, a diterpene synthase, a sesquiterpene synthase, a sesterterpene synthase, a triterpene synthase, a tetraterpene synthase, and a polyterpene synthase.

26. The method of claim 1, wherein $(N)_x$ is provided as an expression vector comprising a nucleic acid sequence encoding $(N)_x$.

27. The method of claim 1, wherein $(N)_x$ is transformed into the host cell as a purified protein.

28. The method of claim 1, wherein $(N)_x$ is selected from the group consisting of an endonuclease, a zinc finger nuclease, a TAL-effector DNA binding domain-nuclease fusion protein (TALEN), a transposase, and a site-specific recombinase.

29. The method of claim 28, wherein the zinc finger nuclease is a fusion protein comprising the cleavage domain of a TypeIIS restriction endonuclease fused to an engineered zinc finger binding domain.

30. The method of claim 29, wherein the TypeIIS restriction endonuclease is selected from the group consisting of HO endonuclease and Fok I endonuclease.

31. The method of claim 29, wherein the zinc finger binding domain comprises 3, 5 or 6 zinc fingers.

32. The method of claim 30, wherein the endonuclease is a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

33. The method of claim 30, wherein the endonuclease is selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

34. The method of claim 28, wherein the endonuclease is modified to specifically bind an endogenous genomic sequence, wherein the modified endonuclease no longer binds to its wild type endonuclease recognition sequence.

35. The method of claim 34, wherein the modified endonuclease is derived from a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

36. The method of claim 34, wherein the modified endonuclease is derived from an endonuclease selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-

PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

37. The method of claim 1, wherein the host cell is selected from the group consisting of a fungal cell, a bacterial cell, a plant cell, and an animal cell.

38. The method of claim 1, wherein the host cell is a yeast cell.

39. The method of claim 38, wherein the yeast cell is a *Saccharomyces cerevisiae* cell.

40. The method of claim 39, wherein the *Saccharomyces cerevisiae* cell is of the Baker's yeast, Mauri, Santa Fe, IZ-1904, TA, BG-1 , CR-1, SA-1, M-26, Y-904, PE-2, PE-5, VR-1, BR-1, BR-2, ME-2, VR-2, MA-3, MA-4, CAT-1, CB-1, NR-1, BT-1 or AL-1 strain.

41. A host cell generated by the method of claim 1.

42. A host cell comprising:

(a) a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid $(ES)_x$ comprises a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a target site $(TS)_x$ of said host cell genome; and

(b) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$;

wherein x is any integer from 1 to n wherein n is at least 2.

43. The host cell of claim 42, wherein $(HR1)_x$ is homologous to a 5' region of $(TS)_x$, and $(HR2)_x$ is homologous to a 3' region of $(TS)_x$.

44. The host cell of claim 33, wherein $(N)_x$ is capable of cleaving at a region positioned between said 5' and 3' regions of $(TS)_x$.

45. The host cell of claim 42, wherein a single nuclease is capable of cleaving each $(TS)_x$.

46. The host cell of claim 42, wherein n= 3, 4, 5, 6, 7, 8, 9 or 10.

47. The host cell of claim 42, wherein $(N)_x$ is capable of cleaving an endogenous genomic sequence within $(TS)_x$.

48. The host cell of claim 42, wherein $(N)_x$ is capable of cleaving an exogenous sequence within $(TS)_x$, wherein x is 1 or any integer from 1 to n.

49. The host cell of claim 42, wherein the exogenous sequence is a recognition sequence for a homing endonuclease.

50. The host cell of claim 42, wherein the homing endonuclease is F-OphI.

51. The host cell of claim 42, wherein $(ES)_x$ further comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$.

52. The host cell of claim 51, wherein $(D)_x$ is selected from the group consisting of a selectable marker, a promoter, a nucleic acid sequence encoding an epitope tag, a gene of interest, a reporter gene, and a nucleic acid sequence encoding a termination codon.

53. The host cell of claim 42, wherein $(ES)_x$ is linear.

54. The host cell of claim 42, wherein the host cell comprises one or more heterologous nucleotide sequences encoding one or more enzymes of a biosynthetic pathway.

55. The host cell of claim 54, wherein the one or more heterologous nucleotide sequences encoding one or more enzymes of a biosynthetic pathway are genomically integrated.

56. The host cell of claim 42, wherein each said exogenous nucleic acid $(ES)_x$ comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$, encoding an enzyme of a biosynthetic pathway.

57. The host cell of claim 56, wherein $(D)_x$ is a member of a library $(L)_x$ comprising a plurality of nucleic acid molecules that encode variants of an enzyme of a biosynthetic pathway.

58. The host cell of claim 42, wherein the host cell comprises one or more heterologous nucleotide sequences encoding one or more enzymes of a mevalonate (MEV) pathway for making isopentenyl pyrophosphate.

59. The host cell of claim 58, wherein the one or more enzymes of the mevaloante pathway are selected from acetyl-CoA thiolase, HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, phosphomevalonate kinase and mevalonate pyrophosphate decarboxylase.

60. The host cell of claim 58, wherein the host cell comprises a plurality of heterologous nucleic acids encoding each of the enzymes of a MEV pathway.

61. The host cell of claim 58, wherein each said exogenous nucleic acid $(ES)_x$ comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$, encoding a terpene synthase.

62. The host cell of claim 61, wherein the terpene synthase is selected from the group consisting of a monoterpene synthase, a diterpene synthase, a sesquiterpene synthase, a sesterterpene synthase, a triterpene synthase, a tetraterpene synthase, and a polyterpene synthase.

63. The host cell of claim 42, wherein $(N)_x$ is provided as an expression vector comprising a nucleic acid sequence encoding $(N)_x$.

64. The host cell of claim 42, wherein $(N)_x$ is transformed into the host cell as a purified protein.

65. The host cell of claim 42, wherein $(N)_x$ is transformed into the host cell as a purified RNA.

66. The host cell of claim 42, wherein $(N)_x$ is selected from the group consisting of an endonuclease, a zinc finger nuclease, a TAL-effector DNA binding domain-nuclease fusion protein (TALEN), a transposase, and a site-specific recombinase.

67. The host cell of claim 66, wherein the zinc finger nuclease is a fusion protein comprising the cleavage domain of a TypeIIS restriction endonuclease fused to an engineered zinc finger binding domain.

68. The host cell of claim 67, wherein the TypeIIS restriction endonuclease is selected from the group consisting of HO endonuclease and Fok I endonuclease.

69. The host cell of claim 67, wherein the zinc finger binding domain comprises 3, 5 or 6 zinc fingers.

70. The host cell of claim 66, wherein the endonuclease is a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

71. The host cell of claim 66, wherein the endonuclease is selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP,

I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiIP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

72. The host cell of claim 66, wherein the endonuclease is modified to specifically bind an endogenous host cell genomic sequence, wherein the modified endonuclease no longer binds to its wild type endonuclease recognition sequence.

73. The host cell of claim 72, wherein the modified endonuclease is derived from a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

74. The host cell of claim 72, wherein the modified endonuclease is derived from an endonuclease selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

75. The host cell of claim 42, wherein the host cell is selected from the group consisting of a fungal cell, a bacterial cell, a plant cell, and an animal cell.

76. The host cell of claim 42, wherein the host cell is a yeast cell.

77. The yeast cell of claim 76, wherein the yeast cell is a *Saccharomyces cerevisiae* cell.

78. The yeast cell of claim 77, wherein the *Saccharomyces cerevisiae* cell is of the Baker's yeast, Mauri, Santa Fe, IZ-1904, TA, BG-1, CR-1, SA-1, M-26, Y-904, PE-2, PE-5, VR-1, BR-1, BR-2, ME-2, VR-2, MA-3, MA-4, CAT-1, CB-1, NR-1, BT-1 or AL-1 strain.

79. A kit comprising:

(a) a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid $(ES)_x$ comprises:

(i) a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a selected target site $(TS)_x$ of a yeast cell genome; and

(ii) a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$;

(b) a plurality of nucleases, wherein each nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$;

wherein x is any integer from 1 to n, wherein n is at least 2.

80. The kit of claim 79, further comprising a plurality of primer pairs $(P)_x$, wherein each primer pair is capable of identifying integration of $(ES)_x$ at $(TS)_x$ by PCR.

81. The kit of claim 79, wherein $(HR1)_x$ is homologous to a 5' region of $(TS)_x$, and $(HR2)_x$ is homologous to a 3' region of $(TS)_x$.

82. The kit of claim 79, wherein $(N)_x$ is capable of cleaving at a region positioned between said 5' and 3' regions of $(TS)_x$.

83. The kit of claim 79, wherein n= $\geq$6000, wherein each $(TS)_x$ is a unique region of the yeast cell genome.

84. The kit of claim 79, wherein $(N)_x$ is capable of cleaving an endogenous yeast genomic sequence within $(TS)_x$.

85. The kit of claim 79, wherein $(N)_x$ is capable of cleaving an exogenous sequence within $(TS)_x$.

86. The kit of claim 79, wherein $(ES)_x$ further comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$.

87. The kit of claim 86, wherein $(D)_x$ is selected from the group consisting of a selectable marker, a promoter, a nucleic acid sequence encoding an epitope tag, a gene of interest, a reporter gene, and a nucleic acid sequence encoding a termination codon.

88. The kit of claim 79, wherein $(ES)_x$ is linear.

89. The kit of claim 79, wherein $(ES)_x$ is circular.

90. The kit of claim 79, wherein $(N)_x$ is provided as an expression vector comprising the nucleic acid sequence encoding $(N)_x$.

91. The kit of claim 79, wherein $(N)_x$ is provided as purified protein.

92. The kit of any claim 79, wherein $(N)_x$ is selected from the group consisting of an endonuclease, a zinc finger nuclease, a TAL-effector DNA binding domain-nuclease fusion protein (TALEN), a transposase, and a site-specific recombinase.

93. The kit of claim 92, wherein the zinc finger nuclease is a fusion protein comprising the cleavage domain of a TypeIIS restriction endonuclease fused to an engineered zinc finger binding domain.

94. The kit of claim 93, wherein the TypeIIS restriction endonuclease is selected from the group consisting of HO endonuclease and Fok I endonuclease.

95. The kit of claim 93, wherein the zinc finger binding domain comprises 3, 5 or 6 zinc fingers.

96. The kit of claim 92, wherein the endonuclease is a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

97. The kit of claim 92, wherein the endonuclease is selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-

VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

98. The kit of claim 92, wherein the endonuclease is modified to specifically bind an endogenous yeast genomic sequence, wherein the modified endonuclease no longer binds to its wild type endonuclease recognition sequence.

99. The kit of claim 98, wherein the modified endonuclease is derived from a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

100. The kit of claim 99, wherein the modified endonuclease is derived from an endonuclease selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, I-UarAP, I-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

101. A method for markerless integration of an exogenous nucleic acid into a target site of a yeast cell genome, the method comprising:

(a) contacting a yeast cell with:

(i) an exogenous nucleic acid $(ES)_1$ comprising a first homology region $(HR1)_1$ and a second homology region $(HR2)_1$, wherein $(HR1)_1$ and $(HR2)_1$ are capable of initiating host cell mediated homologous recombination at said target site $(TS)_1$; and

(ii) a nuclease $(N)_1$ capable of cleaving at $(TS)_1$, whereupon said cleaving results in homologous recombination of $(ES)_1$ at $(TS)_1$;

and

(b) recovering a yeast cell having $(ES)_1$ integrated at $(TS)_1$, wherein said recovering does not require integration of a selectable marker.

102. A yeast cell comprising:

(a) an exogenous nucleic acid $(ES)_1$ comprising a first homology region $(HR1)_1$ and a second homology region $(HR2)_1$, wherein $(HR1)_1$ and $(HR2)_1$ are capable of initiating host cell mediated homologous recombination at a target site $(TS)_1$ of the yeast cell genome; and

(b) a nuclease $(N)_1$ capable of cleaving at $(TS)_1$, whereupon said cleaving results in homologous recombination of $(ES)_1$ at $(TS)_1$;

wherein $(ES)_1$ does not comprise a selectable marker.

103. A method for integrating a plurality of exogenous nucleic acids into a host cell genome, the method comprising:

(a) contacting a host cell with:

(i) a plurality of libraries, wherein each library $(L)_x$ comprises a plurality of exogenous nucleic acids, wherein a selected exogenous nucleic acid comprises, in a 5' to 3' orientation, a first homology region $(HR1)_x$, any nucleic acid of interest selected from the group $(D)_x$, and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of said selected exogenous nucleic acid at a target site $(TS)_x$ of said host cell genome; and

(ii) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of said selected exogenous nucleic acid at $(TS)_x$;

and

(b) recovering a host cell wherein an exogenous nucleic acid from each library $(L)_x$ has integrated at each selected target sequence $(TS)_x$,

wherein x is any integer from 1 to n wherein n is at least 2.

104. A host cell comprising:

(a) a plurality of libraries, wherein each library $(L)_x$ comprises a plurality of exogenous nucleic acids, wherein a selected exogenous nucleic acid comprises, in a 5' to 3' orientation, a first homology region $(HR1)_x$, any nucleic acid of interest selected from the group $(D)_x$, and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of

initiating host cell mediated homologous recombination of said selected exogenous nucleic acid at a target site $(TS)_x$ of said host cell genome; and

(b) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of said selected exogenous nucleic acid at $(TS)_x$,

wherein x is any integer from 1 to n wherein n is at least 2.

105. A composition comprising:

(a) a yeast cell;

(b) a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid $(ES)_x$ comprises:

(i) a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a selected target site $(TS)_x$ of a yeast cell genome; and

(ii) a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$;

(c) a plurality of nucleases, wherein each nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$;

wherein x is any integer from 1 to n wherein n is at least 2.

WHAT IS CLAIMED:

1. A method for simultaneously integrating a plurality of (n) exogenous nucleic acids into a plurality of (n) target sites of a host cell genome, wherein n is at least two, the method comprising:

(a) simultaneously contacting a host cell with:

(i) said plurality of exogenous nucleic acids, wherein:

x is an integer that varies from 1 to n, and for each integer x, each exogenous nucleic acid $(ES)_x$ comprises a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a target site $(TS)_x$ selected from said plurality of (n) target sites of said host cell genome; and

(ii) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$;

and

(b) recovering a host cell wherein each exogenous nucleic acid $(ES)_x$ has integrated at its selected target site $(TS)_x$.

2. A host cell comprising:

(a) a plurality of (n) genomic target sites, wherein n is at least two;

(b) a plurality of (n) exogenous nucleic acids, wherein x is an integer that varies from 1 to n, and for each integer x, each exogenous nucleic acid $(ES)_x$ comprises a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a target site $(TS)_x$ selected from said plurality of (n) genomic target sites; and

(c) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of $(ES)_x$ at $(TS)_x$.

3. A host cell comprising:

(a) a plurality of (n) genomic target sites, wherein n is at least two; and

(b) a plurality of (n) exogenous nucleic acids, wherein x is an integer that varies from 1 to n, and for each integer x, each exogenous nucleic acid $(ES)_x$ comprises a first homology region $(HR1)_x$ and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of $(ES)_x$ at a target site $(TS)_x$ selected from said plurality of (n) genomic target sites;

wherein each said genomic target site $(TS)_x$, comprises a double-strand break.

4. The method of claim 1, or the host cell of claim 2 or 3, wherein $(HR1)_x$ is homologous to a 5' region of $(TS)_x$, and $(HR2)_x$, is homologous to a 3' region of $(TS)_x$.

5. The method of claim 1, or the host cell of claim 2, wherein $(N)_x$ is capable of cleaving at a region positioned between said 5' and 3' regions of $(TS)_x$.

6. The method of claim 1, or the host cell of claim 2, wherein a single nuclease is capable of cleaving each $(TS)_x$.

7. The method or host cell of any one of claims 1 to 6, wherein n= 3, 4, 5, 6, 7, 8, 9 or 10.

8. The method of any one of claims 1 and 4 to 7, wherein said recovering does not require integration of a selectable marker.

9. The method of any one of claims 1 and 4 to 7, wherein said recovering occurs at a higher frequency as compared to not contacting the host cell with a nuclease capable of cleaving at said target site.

10. The method of any one of claims 1 and 4 to 7, wherein said recovering occurs at a frequency of about one every 10, 9, 8, 7, 6, 5, 4, 3, or 2 contacted host cells, or clonal populations thereof, screened.

11. The method or host cell of any one of claims 1, 2, and 4 to 10, wherein $(N)_x$ is capable of cleaving an endogenous genomic sequence within $(TS)_x$.

12. The method or host cell of any one of claims 1, 2, and 4 to 10, wherein $(N)_x$ is capable of cleaving an exogenous sequence within $(TS)_x$.

13. The method or host cell of claim 12, wherein the exogenous sequence is a recognition sequence for a homing endonuclease.

14. The method or host cell of claim 13, wherein the homing endonuclease is F-cphI.

15. The method or host cell of any one of claims 1 to 14, wherein $(ES)_x$ further comprises a nucleic acid of interest $(D)_x$ positioned 3' of $(HR1)_x$ and 5' of $(HR2)_x$.

16. The method or host cell of claim 15, wherein $(D)_x$ is selected from the group consisting of a selectable marker, a promoter, a nucleic acid sequence encoding an epitope tag, a gene of interest, a reporter gene, and a nucleic acid sequence encoding a termination codon.

17. The method or host cell of any one of claims 1 to 16, wherein $(ES)_x$ is linear.

18. The method or host cell of any one of claims 1, 2, and 4 to 17, wherein $(N)_x$ is provided as an expression vector comprising a nucleic acid sequence encoding $(N)_x$.

19. The method or host cell of any one of claims 1, 2, and 4 to 18, wherein $(N)_x$ is selected from the group consisting of an endonuclease, a zinc finger nuclease, a TAL-effector DNA binding domain-nuclease fusion protein (TALEN), a transposase, and a site-specific recombinase.

20. The method or host cell of claim 19, wherein the endonuclease is modified to specifically bind an endogenous genomic sequence, wherein the modified endonuclease no longer binds to its wild type endonuclease recognition sequence.

21. The method or host cell of claim 19 or 20, wherein the endonuclease is a homing endonuclease selected from the group consisting of: an LAGLIDADG homing endonuclease, an HNH homing endonuclease, a His-Cys box homing endonuclease, a GIY-YIG homing endonuclease, and a cyanobacterial homing endonuclease.

22. The method of or host cell of claim 19 or 20, wherein the endonuclease is derived from an endonuclease selected from the group consisting of: H-DreI, I-SceI, I-SceII, I-SceIII, I-SceIV, I-SceV, I-SceVI, I-SceVII, I-CeuI, I-CeuAIIP, I-CreI, I-CrepsbIP, I-CrepsbIIP, I-CrepsbIIIP, I-CrepsbIVP, I-TliI, I-PpoI, Pi-PspI, F-SceI, F-SceII, F-SuvI, F-CphI, F-TevI, F-TevII, I-AmaI, I-AniI, I-ChuI, I-CmoeI, I-CpaI, I-CpaII, I-CsmI, I-CvuI, I-CvuAIP, I-DdiI, I-DdiII, I-DirI, I-DmoI, I-HmuI, I-HmuII, I-HsNIP, I-LlaI, I-MsoI, I-NaaI, I-NanI, I-NclIP, I-NgrIP, I-NitI, I-NjaI, I-Nsp236IP, I-PakI, I-PboIP, I-PcuIP, I-PcuAI, I-PcuVI, I-PgrIP, I-PobIP, I-PorI, I-PorIIP, I-PbpIP, I-SpBetaIP, I-ScaI, I-SexIP, I-SneIP, I-SpomI, I-SpomCP, I-SpomIP, I-SpomIIP, I-SquIP, I-Ssp68031, I-SthPhiJP, I-SthPhiST3P, I-SthPhiSTe3bP, I-TdeIP, I-TevI, I-TevII, I-TevIII, i-UarAP, i-UarHGPAIP, I-UarHGPA13P, I-VinIP, I-ZbiIP, PI-MgaI, PI-MtuI, PI-MtuHIP PI-MtuHIIP, PI-PfuI, PI-PfuII, PI-PkoI, PI-PkoII, PI-Rma43812IP, PI-SpBetaIP, PI-SceI, PI-TfuI, PI-TfuII, PI-ThyI, PI-TliI, or PI-TliII.

23. The method or host cell of any one of claims 1 to 22, wherein the host cell is selected from the group consisting of a fungal cell, a bacterial cell, a plant cell, and an animal cell.

24. The method or host cell of any one of claims 1 to 23, wherein the host cell is a yeast cell.

25. The method or host cell of claim 24, wherein the yeast cell is a *Saccharomyces cerevisiae* cell.

26. A method for simultaneously integrating a plurality of (n) exogenous nucleic acids into a plurality of (n) target sites of a host cell genome, wherein n is at least two, the method comprising:

(a) simultaneously contacting a host cell with:

(i) a plurality of libraries, wherein x is an integer that varies from 1 to n, and for each integer x, each library $(L)_x$ comprises a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid comprises, in a 5' to 3' orientation, a first homology region $(HR1)_x$, any nucleic acid of interest selected from the group $(D)_x$, and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of said selected exogenous nucleic acid at a target site $(TS)_x$ of said host cell genome; and

(ii) for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of an exogenous nucleic acid from $(L)_x$ at $(TS)_x$;

and

(b) recovering a host cell wherein an exogenous nucleic acid from each library $(L)_x$ has integrated at each selected target sequence $(TS)_x$.

27. A host cell comprising:

(a) a plurality of (n) genomic target sites, wherein n is at least two;

(b) a plurality of libraries, wherein x is an integer that varies from 1 to n, and for each integer x, each library $(L)_x$ comprises a plurality of exogenous nucleic acids, wherein each exogenous nucleic acid comprises, in a 5' to 3' orientation, a first homology region $(HR1)_x$, any nucleic acid of interest selected from the group $(D)_x$, and a second homology region $(HR2)_x$, wherein $(HR1)_x$ and $(HR2)_x$ are capable of initiating host cell mediated homologous recombination of said selected exogenous nucleic acid at a target site $(TS)_x$ of said host cell genome; and

for each said target site $(TS)_x$, a nuclease $(N)_x$ capable of cleaving at $(TS)_x$, whereupon said cleaving results in homologous recombination of an exogenous nucleic acid from $(L)_x$ at $(TS)_x$.