Claims:

1. A method of making multiple alterations to target DNA in a eukaryotic cell constitutively expressing a Cas9 enzyme that forms a co-localization complex with a guide RNA complementary to the target DNA and that cleaves the target DNA in a site specific manner comprising

(a) introducing into the cell consitutively expressing the Cas9 enzyme a plurality of guide RNAs complementary to different sites of the target DNA, wherein each of the plurality of guide RNAs is a tracrRNA-crRNA fusion, wherein each of the plurality of guide RNAs and the Cas9 enzyme are members of co-localization complexes for the target DNA, wherein the plurality of guide RNAs is introduced without also introducing a foreign nucleic acid encoding the Cas9 enzyme,

introducing into the cell constitutively expressing the Cas9 enzyme a plurality of donor nucleic acid sequences,

wherein at least one of the plurality of guide RNAs and the Cas9 enzyme co-localize to a site of the target DNA, the Cas9 enzyme cleaves the target DNA and one of the plurality of donor nucleic acid sequences is inserted into the target DNA at the site of cleavage to produce altered DNA in the cell, and

(b) repeating step (a) to produce multiple alterations to the DNA in the cell.

2. The method of claim 1 wherein the eukaryotic cell is a yeast cell, a plant cell or an animal cell.

3. The method of claim 1 wherein each of the plurality of guide RNAs is about 100 nucleotides.

4. The method of claim 1 wherein the DNA is genomic DNA, mitochondrial DNA, viral DNA, or exogenous DNA.

5. The method of claim 1 wherein the one of the plurality of donor nucleic acid sequences is inserted by recombination.

6. The method of claim 1 wherein the one of the plurality of donor nucleic acid sequences is inserted by homologous recombination.

7. The method of claim 1 wherein a nucleic acid encoding one or more of each of the plurality of guide RNAs and each of the plurality of donor nucleic acid sequences are present on one or more plasmids.

8. The method of claim 1 wherein the plurality of donor nucleic acid sequences includes homology sequences or arms flanking the site of cleavage.

9. The method of claim 1 wherein each of the plurality of donor nucleic acids includes a sequence to remove the site of cleavage.