CLAIMS

1. A method of altering two or more target nucleic acids in a cell comprising

introducing into the cell a first foreign nucleic acid encoding two or more guide RNAs complementary to the two or more target nucleic acids,

introducing into the cell a second foreign nucleic acid encoding two or more orthogonal RNA guided DNA binding proteins of a Type II CRISPR system,

wherein the two or more guide RNAs and the two or more orthogonal RNA guided DNA binding proteins of the Type II CRISPR system are expressed,

wherein two or more co-localization complexes form with each including a guide RNA and an orthogonal RNA guided DNA binding protein of the Type II CRISPR system and a target nucleic acid and wherein the orthogonal RNA guided DNA binding protein of the Type II CRISPR system cuts or nicks the target nucleic acid.

2. The method of claim 1 wherein the two or more orthogonal RNA guided DNA binding proteins of the Type II CRISPR system are nucleases.

3. The method of claim 1 wherein the two or more orthogonal RNA guided DNA binding proteins of the Type II CRISPR system are nickases.

4. The method of claim 1 wherein the two or more orthogonal RNA guided DNA binding proteins of the Type II CRISPR system comprise a nuclease or a nickase.

5. The method of claim 1 wherein the cell is a eukaryotic cell.

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

7. The method of claim 1 wherein each guide RNA is between about 10 to about 500 nucleotides.

8. The method of claim 1 wherein each guide RNA is between about 20 to about 100 nucleotides.

9. The method of claim 1 wherein each guide RNA is between about 100 to about 500 nucleotides.

10. The method of claim 1 wherein each guide RNA is a crRNA fused to a tracrRNA.

11. The method of claim 1 wherein a target nucleic acid is genomic DNA, mitochondrial DNA, viral DNA, or exogenous DNA.

12. The method of claim 1 wherein a plurality of target nucleic acids is cut or nicked.

13. The method of claim 1 wherein each orthogonal RNA guided DNA binding protein of the Type II CRISPR system is an orthogonal Cas9 protein.