any of the appended Tables and Figures, including any combination of these mutants with each other and with other mutants (such as dimerization and/or catalytic domain mutants as well as nickase mutations). Mutations as described herein, include but are not limited to, mutations that change the charge of the cleavage domain, for example mutations of positively charged residues to non-positively charged residues (*e.g.*, mutations of K and R residues (*e.g.*, mutated to S); N residues (*e.g.*, to D), and Q residues (*e.g.*, to E); mutations to residues that are predicted to be close to the DNA backbone based on molecular modeling and that show variation in *Fok*I homologs (Figures 1 and 17); and/or mutations at other residues (*e.g.*, U.S. Patent No. 8,623,618 and Guo *et al*, (2010) *J. Mol. Biol*. 400(1):96-107).

[0012a] In one aspect, provided herein is a zinc finger protein comprising at least three zinc finger DNA-binding domains, wherein each zinc finger DNA-binding domain comprises two beta sheets, an alpha helix region, a recognition helix region that binds to a nucleotide sequence, and further wherein one or more of the zinc finger DNA-binding domains comprise mutations in amino acid residues at any one of positions (-5), (-9) and/or (-14), numbered relative to the start of the alpha helix region, and wherein the amino acid residues at positions (-5), (-9) and/or (-14) are mutated to an alanine (A), a leucine (L), a serine (S), an aspartic acid (N), glutamine (E), tyrosine (Y) and/or glutamine (Q) residue.

[0012b] In another aspect, provided herein is a zinc finger nuclease comprising the zinc finger protein as described herein and a cleavage domain.

[0012c] In another aspect, provided herein is a zinc finger nuclease comprising a first and a second dimerizing zinc finger nuclease as described herein and a second zinc finger nuclease.

[0012d] In another aspect, provided herein is one or more polynucleotides encoding the zinc finger protein as described herein or the zinc finger nuclease as described herein.

[0012e] In yet another aspect, provided herein is an isolated cell comprising the one or more polynucleotides as described herein.

[0012f] In yet another aspect, provided herein is an *in vitro* method for cleaving genomic cellular chromatin in a region of interest, the method comprising:

expressing the zinc finger nuclease as described herein or the one or more polynucleotides as described herein in a cell *in vitro*,

wherein the zinc finger nuclease site-specifically cleaves a nucleotide sequence in the region of interest of the genomic cellular chromatin.

[0012g] In yet another aspect, provided herein is an isolated cell or cell line comprising the zinc finger protein as described herein, the zinc finger nuclease as described herein and/or the one or more polynucleotides as described herein.

[0012h] In another aspect, provided herein is a composition comprising first and second polynucleotides encoding the first and second zinc finger nucleases as described herein, wherein the first polynucleotide encodes the first zinc finger nuclease and the second polynucleotide encodes the second zinc finger nuclease and the ratio of the first and second zinc finger nucleases is not one to one, optionally a ratio of 1:2, 1:3, 1:4, 1:5, 1:6, 1:8, 1:9, 1:10, 1:20 or 1:30 ratio.

[0013] The most promising mutations were found using the second criteria. The initial promising mutations were positively charged residues predicted to be close to the DNA backbone when *Fok*I is bound to DNA. The cleavage domains described herein may include one, two, three, four, five or more of the mutations described herein and may further include additional known mutations. Therefore, mutations of the invention do not include specific mutations disclosed in U.S. Patent No. 8,623,618 (*e.g.,* N527D, S418P, K448M, Q531R, etc.) when used alone; however, provided here are novel mutants that can be used in combination with the mutants of U.S. Patent No. 8,623,618. Nickase mutants wherein one of the catalytic nuclease domains in a dimer pair comprises one or more mutations rendering it catalytically inactive (see U.S. Patent Nos 8,703,489; 9,200,266; and 9,631,186) may also be used in combination with any of the mutants described herein. Nickases can be ZFN nickases, TALEN nickases and CRISPR/dCas systems.

[0014] In certain embodiments, the engineered cleavage half domains are derived from *Fok*I or *Fok*I homologues and comprise a mutation in one or more of amino acid residues 416, 422, 447, 448, and/or 525, numbered relative to the wild-type full length *Fok*I as shown in SEQ ID NO:1 or corresponding residues in *Fok*I homologues (see, Figure 17). In other embodiments, the cleavage half domains derived from *FokI* comprises a mutation in one or more of amino acid residues 414-426, 443-450, 467-488, 501-502, and/or 521-531, including one or more of 387, 393, 394, 398, 400, 416, 418, 422, 427, 434, 439, 441, 442, 444, 446, 448, 472, 473, 476, 478, 479, 480, 481, 487, 495, 497, 506, 516, 523, 525, 527, 529, 534, 559, 569, 570, and/or 571. The mutations may include mutations to residues found in natural restriction enzymes homologous to *Fok*I at the corresponding positions (Figure 17).