CLAIMS

What is claimed is:

~~1. A fusion protein comprising a DNA-binding domain and at least one catalytically inactive cleavage domain or cleavage half-domain.~~

~~2. The fusion protein of claim 1, wherein the DNA-binding domain comprises a zinc finger domain.~~

~~3. The fusion protein of claim 2, wherein the zinc finger domain is non-naturally occurring.~~

~~4. The fusion protein of any of claims 1 to 3, wherein the cleavage domain is a *FokI* cleavage half-domain.~~

~~5. A polynucleotide encoding the fusion protein of any of claims 1 to 4.~~

~~6. A protein complex comprising the fusion protein of any of claims 1 to 4 and a second fusion protein comprising a zinc finger domain and a catalytically active cleavage half-domain, wherein the catalytically inactive cleavage half-domain forms a heterodimer with the catalytically active cleavage half-domain of the second fusion protein.~~1. A protein complex comprising:

(a) a first fusion protein comprising a DNA-binding domain and at least one catalytically inactive *FokI* cleavage domain or cleavage half-domain, wherein the cleavage domain or cleavage half-domain comprises a mutation at one or more of amino acid residues 450, 467 and 469; and

(b) a second fusion protein comprising a zinc finger domain and a *FokI* catalytically active cleavage half domain,

wherein the catalytically inactive *FokI* cleavage half domain forms a heterodimer with the catalytically active *FokI* cleavage half-domain of the second fusion protein and further wherein the protein complex induces a single-stranded break in a target double-stranded sequence.

~~7~~2. A composition comprising ~~the polynucleotide of~~a protein complex according to claim ~~5~~ 1 or one or more polynucleotides encoding the first and/or second fusion proteins of the protein complex of claim 1~~and a second polynucleotide encoding a fusion protein comprising a zinc finger domain and a catalytically active cleavage half-domain, wherein the catalytically inactive cleavage half-domain forms a heterodimer with the catalytically active cleavage half-domain of the second fusion protein~~.

~~8~~3. An isolated cell or cell line comprising ~~a fusion protein according to any of claims 1 to 4, a polynucleotide according to claim 5,~~ a protein complex according to claim ~~6~~1 ~~and/or a composition according to claim 7~~.

~~94~~. An *in vitro* method of generating a single-stranded break in a target double-stranded sequence in a cell, the method comprising:

providing a protein complex according to claim ~~6~~ 1 ~~or a composition according to claim 7~~, wherein the heterodimer generates a single-stranded break in the target double-stranded sequence.

~~105~~. The method of claim ~~93~~, wherein the target sequence is in cellular chromatin.

~~116~~. An *in vitro* method of inserting an exogenous sequence into a region of interest in a cell, the method comprising

generating a single-stranded break in the region of interest according to the method of claim ~~94~~; and

providing an exogenous sequence that is inserted into the region of interest following generation of a single-stranded break.

~~127~~. The method of claim ~~116~~, wherein the exogenous sequence replaces a wild-type genomic sequence.

~~138~~. An *in vitro* method of inactivating a target sequence in a region of interest of a cell, the method comprising

generating a single-stranded break in the region of interest according to the method of claim ~~94~~, and

providing an exogenous sequence that replaces the wild-type sequence in the region of interest and wherein the exogenous sequence partially or fully inactivates the target sequence.