

CLAIMS

1. A hybrid meganuclease comprising a first domain and a second domain in the orientation N-terminal toward C-terminal, wherein said first domain is derived from the N-terminal domain of I-DmoI and said second domain is derived from ~~I-CreI~~, said first and second domains being bound by a convenient linker, each domain being a polypeptide fragment comprising or consisting of a dodecapeptide motif and a DNA binding moiety, and wherein said hybrid meganuclease is capable of causing DNA cleavage.
2. Hybrid meganuclease according to claim 1, wherein said convenient linker comprises a loop derived from a di-dodecapeptide meganuclease.
3. Hybrid meganuclease according to claim 1 or 2, wherein said convenient linker comprises a loop derived from said first di-dodecapeptide meganuclease or a part thereof.
4. Hybrid meganuclease according to claims 1 to 3, wherein said hybrid meganuclease comprises the sequence of SEQ ID NO :4.
5. A purified or recombinant polynucleotide encoding a meganuclease according to any one of claims 1-4.
6. A purified or recombinant polynucleotide comprising a hybrid target and cleavage site for a meganuclease according to any of claims 1-4.
7. Polynucleotide according to claim 6, wherein said site comprises two half-sites of the initial dodecapeptide meganuclease.
8. A vector comprising a polynucleotide according to any of claims 5-7.
9. A host cell comprising a polynucleotide according to any of claims 5-7, a vector according to claim 8 or a meganuclease according to anyone of claims 1-4.
10. Use of a polynucleotide according to any of claims 5-7, a vector according to claim 8 or a meganuclease according to any of claims 1-4 as a molecular biology tool.
11. Use of a polynucleotide according to any of claims 5-7, a vector according to claim 8 or a meganuclease according to any of claims 1-4 for genetic

engineering, provided that the germline genetic identity of human beings is not modified.

12. A method of genetic engineering comprising the steps of:

5 1) introducing a double-strand break at the targeting locus comprising the hybrid target site with the corresponding meganuclease according to any of claims 1-4 ; and

2) providing a targeting construct comprising the sequence to introduce flanked by homologous sequence to the targeting locus.

10 13. Method according to claim 12, wherein said targeting locus is a genomic locus.

14. Method according to any of claims 12-13, wherein said meganuclease is provided either by an expression vector comprising a polynucleotide according to claim 5 or by said meganuclease itself.

15 15. A method of deleting a viral genome or a part thereof, wherein a double-strand break in the viral genome is induced by a meganuclease according to any of claims 1-4 and said double-strand break induces a recombination event leading to the deletion of the viral genome or a part thereof.