CLAIMS

1. An isolated Cas protein or polypeptide fragment, having an amino acid sequence of SEQ ID NO: 1 or a sequence of at least 77% identity therewith, wherein the Cas protein is capable of cleaving a polynucleotide comprising a target nucleic acid sequence between 50°C and 100°C, when associated with at least one RNA molecule which recognizes the target sequence.

2. A Cas protein or polypeptide fragment as claimed in claim 1, wherein the Cas protein or fragment is capable of nucleic acid cleavage between 50°C and 75°C, preferably above 60°C; more preferably between 60°C and 80°C; even more preferably between 60°C and 65°C.

3. A Cas protein or polypeptide fragment as claimed in claim 1 or claim 2, wherein the nucleic acid cleavage is DNA cleavage.

4. A Cas protein or polypeptide fragment as claimed in any preceding claim, wherein the Cas protein is obtainable from a bacterium, archaeon or virus.

5. A Cas protein or polypeptide fragment as claimed in any preceding claim, wherein the Cas protein is obtainable from *Geobacillus* sp., preferably from *Geobacillus thermodenitrificans*.

6. A ribonucleoprotein complex comprising a Cas protein as claimed in any preceding claim, and comprising at least one targeting RNA molecule which recognises a sequence in a target polynucleotide.

7. A ribonucleoprotein complex as claimed in claim 6, wherein the targeting RNA molecule comprises a crRNA and optionally a tracrRNA.

8. A ribonucleoprotein complex as claimed in claim 6 or claim 7, wherein the length of the at least one RNA molecule is in the range 35 – 135 nucleotide residues.

9. A ribonucleoprotein complex as claimed in claim 6 or claim 7, wherein the target sequence is 31 or 32 nucleotide residues in length.

10. A Cas protein or polypeptide as claimed in any of claims 1 to 5 or a ribonucleoprotein complex as claimed in any of claims 6 to 9, wherein the protein or polypeptide is provided as part of a protein complex comprising at least one further functional or non-functional protein.

11. A Cas protein, polypeptide, or ribonucleoprotein complex as claimed in claim 10, wherein the Cas protein or polypeptide, and/or the at least one further protein further comprise at least one functional moiety.

12. A Cas protein or polypeptide, or ribonucleoprotein complex as claimed in claim 11, wherein the at least one functional moiety is fused or linked to the N-terminus and/or the C-terminus of the Cas protein, polypeptide or ribonucleoprotein complex; preferably the N-terminus.

13. A Cas protein or polypeptide, or a ribonucleoprotein complex as claimed in claim 11 or claim 12, wherein the at least one functional moiety is a protein; optionally selected from a helicase, a nuclease, a helicase-nuclease, a DNA methylase, a histone methylase, an acetylase, a phosphatase, a kinase, a transcription (co-)activator, a transcription repressor, a DNA binding protein, a DNA

structuring protein, a marker protein, a reporter protein, a fluorescent protein, a ligand binding protein, a signal peptide, a subcellular localisation sequence, an antibody epitope or an affinity purification tag.

14. A Cas protein or polypeptide, or a ribonucleoprotein complex as claimed in claim 13, wherein the native activity of the Cas9 nuclease is inactivated and the Cas protein is linked to at least one functional moiety.

15. A Cas protein or polypeptide, or a ribonucleoprotein complex as claimed in claim 13 or claim 14, wherein the at least one functional moiety is a nuclease domain; preferably a FokI nuclease domain.

16. A Cas protein or polypeptide, or a ribonucleoprotein complex as claimed in any of claims 13 to 15, wherein the at least one functional moiety is a marker protein.

17. An isolated nucleic acid molecule encoding a clustered regularly interspaced short palindromic repeat (CRISPR)-associated (Cas) protein having an amino acid sequence of SEQ ID NO: 1 or a sequence of at least 77% identity therewith; or a polypeptide fragment thereof.

18. An isolated nucleic acid molecule as claimed in claim 17, further comprising at least one nucleic acid sequence encoding an amino acid sequence which upon translation is fused with the Cas protein or polypeptide.

19. An isolated nucleic acid molecule as claimed in claim 18, wherein the at least one nucleic acid sequence fused to the nucleic acid molecule encoding the Cas protein or polypeptide, encodes a protein selected from a protein selected from a helicase, a nuclease, a helicase-nuclease, a DNA methylase, a histone methylase,

an acetylase, a phosphatase, a kinase, a transcription (co-)activator, a transcription repressor, a DNA binding protein, a DNA structuring protein, a marker protein, a reporter protein, a fluorescent protein, a ligand binding protein, a signal peptide, a subcellular localisation sequence, an antibody epitope or an affinity purification tag.

20. An expression vector comprising a nucleic acid molecule as claimed in any of claims 17 to 19.

21. An expression vector as claimed in claim 20, further comprising a nucleotide sequence encoding at least one targeting RNA molecule.

22. A method of modifying a target nucleic acid comprising contacting the nucleic acid with:

a. a ribonucleoprotein complex of any of claims 6 to 9; or

b. a protein or protein complex of any of claims 10 to 16 and at least one targeting RNA molecule as defined in any of claims 4 to 9.

23. A method of modifying a target nucleic acid in a cell, comprising transforming, transfecting or transducing the cell with an expression vector of claim 21; or alternatively transforming, transfecting or transducing the cell with an expression vector of claim 20 and a further expression vector comprising a nucleotide sequence encoding a targeting RNA molecule as defined in any of claims 4 to 9.

24. A method of modifying a target nucleic acid in a cell comprising transforming, transfecting or transducing the cell with an expression vector of claim 20, and then delivering a targeting RNA molecule as defined in any of claims 4 to 9 to, or into the cell.

25. A method of modifying a target nucleic acid as claimed in any of claims 22 to 24, wherein the at least one functional moiety is a marker protein or reporter protein and the marker protein or reporter protein associates with the target nucleic acid; preferably wherein the marker is a fluorescent protein, for example a green fluorescent protein (GFP).

26. A method as claimed in any of claims 22 to 25, wherein the target nucleic acid is DNA; preferably dsDNA.

27. A method as claimed in any of claims 22 to 25, wherein the target nucleic acid is RNA.

28. A method of modifying a target nucleic acid as claimed in claim 26, wherein the nucleic acid is dsDNA, the at least one functional moiety is a nuclease or a helicase-nuclease, and the modification is a single-stranded or a double-stranded break at a desired locus.

29. A method of silencing gene expression at a desired locus according to any of the methods as claimed in claims 23, 24, 26 or 28.

30. A method of modifying or deleting and/or inserting a desired nucleotide sequence at a desired location according to any of the methods as claimed in claims 23, 24, 26 or 28.

31. A method of modifying gene expression in a cell comprising modifying a target nucleic acid sequence as claimed in a method of any of claims 22 to 26; wherein the

nucleic acid is dsDNA and the functional moiety is selected from a DNA modifying enzyme (e.g. a methylase or acetylase), a transcription activator or a transcription repressor.

32. A method of modifying gene expression in a cell comprising modifying a target nucleic acid sequence as claimed in a method of claim 27, wherein the nucleic acid is an mRNA and the functional moiety is a ribonuclease; optionally selected from an endonuclease, a 3' exonuclease or a 5' exonuclease.

33. A method of modifying a target nucleic acid as claimed in any of claims 22 to 32, wherein the method is carried out at a temperature between 50°C and 100°C.

34. A method of modifying a target nucleic acid as claimed in claim 33, wherein the method is carried out at a temperature at or above 60°C, preferably between 60°C and 80°C, more preferably between 60°C and 65°C.

35. A method as claimed in any of claims 22 to 34 wherein the cell is a prokaryotic cell.

36. A method as claimed in any of claims 22 to 35 wherein the cell is a eukaryotic cell.

37. A host cell transformed by a method as claimed in any of claims 22 to 33.