Claims

1. In vitro use of a combination of

(a) at least one compound (III) which is a DNA-PK inhibitor, and

(b) at least one compound (I) which is an HDAC inhibitor, at least one compound (II) which is an NAE inhibitor and/or at least one compound (IV) which is an RPA inhibitor,

for genome editing in an eukaryotic target cell, particularly in a mammalian target cell, more particularly in a human target cell, wherein the genome editing comprises introducing a staggered cut into the double-stranded genome of the target cell.

2. The use of claim 1

wherein the compound (I) is Trichostatin A, and/or

the compound (II) is MLN4924, and/or
the compound (III) is NU7026 and/or

the compound (IV) is NSC15520.

3. The use of claim 1 and 2 wherein the combination comprises

- at least one compound (III),

- at least one compound (I) and/or

- at least one compound (II) and

- optionally at least one compound (IV).

4. The use of any one of claims 1-3 wherein the genome editing comprises introducing a staggered cut with 5’ overhangs into the double-stranded genome of the target cell.

5. The use of any one of claims 1-4 wherein the genome editing comprises (i) the presence of a CRISPR/Cas9D10A enzyme in the target cell, or (ii) the presence of CRISPR/Cpf1 enzyme in the target cell.

6. The use of any one of claims 1-5 for genome editing in a stem cell, including an induced or embryonic pluripotent stem cell of an eukaryotic target organism, particularly a human induced or embryonic pluripotent stem cell.

7. The use of claim 6 wherein the combination comprises at least one compound (III), at least one compound (I), at least one compound (II) and at least one compound (IV).

8. The use of any one of claims 1-5 for genome editing in a hematopoietic cell, or in a hematopoietic progenitor cell.

9. The use of claim 8 wherein the combination comprises at least one compound (III), at least one compound (I) and optionally at least one compound (IV), particularly in the absence of a compound (II).

10. The use of any one of claims 1-5 for genome editing in an immortalized cell.

11. The use of claim 10 wherein the combination comprises at least one compound (III), at least one compound (I) and at least one compound (IV), particularly in the absence of compound (II).

12. The use of any one of claims 1-11 wherein the combination further comprises

(i) a DNA protein kinase catalytic subunit which is catalytically inactive, but structurally intact; and which comprises at least one mutation compared to the wild-type sequence, particularly the mutated subunit K3753R,

(ii) a nucleic acid molecule encoding the DNA protein kinase catalytic subunit (i) and/or

(iii) a eukaryotic cell capable of expressing the DNA protein kinase catalytic subunit of (i).

13. The use of any one of claims 1-12 wherein the genome editing comprises introcuding a donor DNA molecule carrying a desired mutation, which is a single-stranded or double-stranded DNA molecule, particularly a single-stranded DNA molecule, into the target cell.

14. A combination comprising

(a) at least one compound (III) which is a DNA-PK inhibitor, and

(b) at least one compound (I) which is an HDAC inhibitor, at least one compound (II) which is an NAE inhibitor and/or at least one compound (IV) which is an RPA inhibitor,

for use in medicine including human or veterinary medicine in a method comprising genome editing in a eukaryotic target cell or target organism, particularly in a mammalian target cell or target organism, more particularly in a human target cell or target organism, wherein the genome editing comprises introducing a staggered cut into the double-stranded genome of the target cell or target organism.

15. A method for editing the genome of an eukaryotic target cell or target organism, comprising introducing a combination

(a) at least one compound (III) which is a DNA-PK inhibitor, and

(b) at least one compound (I) which is an HDAC inhibitor, at least one compound (II) which is an NAE inhibitor and/or at least one compound (IV) which is an RPA inhibitor,

into the target cell or target organism wherein the genome editing comprises introducing a staggered cut into the double-stranded genome of the target cell or target organism.