CLAIMS

1. An ex vivo or in vitro method for site-specific sequence modification of a target genomic DNA region in cells comprising:

transfecting the cells by electroporation with a composition comprising (a) a single-stranded DNA oligo; (b) a DNA digesting agent encoded on a RNA; and (c) a targeting RNA, wherein the targeting RNA is capped and/or polyadenylated;

wherein the DNA oligo comprises:

(i) a homologous region comprising DNA sequence homologous to the target genomic DNA region; and

(ii) a sequence modification region; and

wherein the genomic DNA sequence is modified specifically at the target genomic DNA region and wherein the DNA oligo and the targeting RNA are complementary to the same strand of the target genomic DNA region.

2. The method of claim 1, wherein electroporation is flow electroporation using a flow electroporation device.

3. The method of claim 1 or 2, wherein the DNA digesting agent comprises Cas9.

4. The method of any one of claims 1-3, wherein the DNA digesting agent comprises a site-specific nuclease.

5. The method of any one of claims 1-4, wherein the targeting RNA comprises a guide RNA.

6. The method of any one of claims 1-5, wherein the DNA oligo is 10-50 nucleic acids.

7. The method of any one of claims 1-6, wherein the concentration of the DNA oligo in the composition is from 35 to 200 μg/mL.

8. The method of any one of claims 1-7, wherein the composition is non-viral.

9. The method of any one of claims 1-8, wherein the cells comprise mammalian cells and wherein the mammalian cells comprise peripheral blood lymphocytes, B cells, expanded T cells, hematopoietic stem cells, or mesenchymal stem cells.

10. The method of claim 9, wherein the mammalian cells are primary mammalian cells.

11. The method of any one of claims 1-8, wherein the cells are cells isolated from a patient.

12. The method of claim 11, wherein the cell viability after electroporation is at least 40%.

13. The method of claim 11 or 12, wherein the cells are isolated from the bone marrow of the subject.

14. The method of any one of claims 11-13, wherein the cells comprise stem cells or hematopoietic stem cells.

15. The method of 9 or 10, wherein the cells are cells isolated from a patient.

16. The method of claim 15, wherein the cell viability after electroporation is at least 40%.

17. The method of claim 15 or 16, wherein the cells are isolated from the bone marrow of the subject.