CLAIMS:

1. A guided nuclease system for use in a method of treating or reducing a disease or condition in a patient, wherein the method comprises modulating immune cells in the patient by altering a microbiota of the patient using a guided nuclease of the system, wherein the disease or condition is mediated by immune cells (eg, T-cells) or treated or prevented by altering immune cell activities or populations in the patient.
2. The system of claim 1, wherein the method comprises selective targeting of the genome of cells of a first species in the microbiota using the guided nuclease to effect the alteration.
3. The system of claim 2, wherein the selective targeting avoids targeting of (i) species of the same phylum as said first species, or (ii) a different strain of the first species.
4. The system of any preceding claim, wherein the method selectively kills first cells in the microbiota whilst not targeting second cells, wherein the second cells are (i) of a related strain to the strain of the first species or (ii) of a species that is different to the first species and is phylogenetically related to the first species, wherein the second species or strain has a 16s ribosomal RNA-encoding DNA sequence that is at least 80% identical to an 16s ribosomal RNA-encoding DNA sequence of the first cell species or strain, wherein the growth of the second cells in the microbiota is not inhibited by said method or the growth of said first cells is inhibited by at least 5x the growth inhibition of the second cells.
5. The system of any preceding claim, wherein
   (a) the patient is a human patient;
   (b) the microbiota is a gut microbiota;
   (c) the method comprises selective targeting of the genome of a first species in the microbiota using the guided nuclease to effect the alteration; and
   (d) wherein the method selectively kills first cells in the microbiota whilst not targeting second cells, wherein the second cells are (a) of a related strain to the strain of the first species or (b) of a species that is different to the first species and is phylogenetically related to the first species, wherein the second species or strain has a 16s ribosomal RNA-encoding DNA sequence that is at least 80% identical to an 16s ribosomal RNA-encoding DNA sequence of the first cell species or strain.
6. An *ex vivo* population of immune cells for use in a method of adoptive cell therapy of a patient for treating or preventing a disease or condition in the patient, the method comprising

(a) Carrying out adoptive immune cell therapy in the patient, comprising administering cells of said population to the patient, wherein administration of said immune cells is capable of treating the disease or condition in the patient; and

(b) Altering the relative proportion of a sub-population of cells of a first bacterial species or strain, or archaeal species or strain, in the gut microbiota of the patient, thereby producing an altered gut microbiota that modulates the immune cell therapy in the patient;

wherein step (b) is carried out by targeting the sub-population of first cells by administering thereto an anti-bacterial or anti-archaeal guided nuclease system simultaneously or sequentially with said immune cell population, whereby first cells are killed or the sub-population growth is reduced, thereby reducing the proportion of said sub-population in the gut microbiota of the patient.

7. The system or population of any one of claims 2 to 6, wherein the first cells are bacterial or archaeal cells, eg, *Firmicutes* cells.
8. The system or population of any one of claims 2 to 7, wherein the method comprises modifying (eg, cutting and/or mutating) one or more target genomic or episomal nucleotide sequences of cells of the first species.
9. The system or population of any one of claims 2 to 8, wherein the first cells comprise a population of host cells, the method comprising modifying a target sequence in the host cells, wherein the target sequence modification is carried out by
    a. combining the microbiota with multiple copies of engineered nucleic acid sequences encoding host modifying (HM) crRNAs, and
    b. expressing HM-crRNAs in host cells,

    wherein each engineered nucleic acid sequence is operable with a Cas nuclease in a respective host cell to form a HM-CRISPR/Cas system and the engineered sequence comprises
    (i) spacer and repeat sequences encoding a HM-crRNA;
    (ii) the HM-crRNA comprising a sequence that is capable of hybridizing to a host cell target sequence to guide Cas nuclease to the target sequence in the host cell; and

    optionally the HM-system comprises a tracrRNA sequence or a DNA sequence expressing a tracrRNA sequence;

    whereby HM-crRNAs guide Cas modification of host target sequences in host cells, whereby host cells are killed or the host cell population growth is reduced, thereby reducing the proportion of said first cells in the microbiota.
10. The system of any one of claims 1 to 5 and 7 to 9, wherein the modulated immune cells comprise endogenous cells of the patient and/or administered cells, such as *via* adoptive cell therapy.

11. The system or population of any preceding claim, wherein the nuclease is a RNA-guided nuclease.
12. The system or population of any preceding claim, wherein the system is an engineered CRISPR/Cas system, TALEN system, meganuclease system or zinc finger system.
13. The system or population of any preceding claim, wherein the method (i) upregulates a T_H1, T_H17 and/or T_{reg} cell population; or (ii) downregulates a T_H1, T_H17 and/or T_{reg} cell population in the patient.
14. The system or population of any preceding claim, wherein the method is a method of modulating a therapy of the disease or condition in the patient, the method comprising
    (a) carrying out the therapy in the patient; and
    (b) causing gut bacterial microbiota dysbiosis in the patient by carrying out said altering of the microbiota using the guided nuclease, whereby said dysbiosis modulates the therapy in the patient by said modulating of immune cells in the patient.
15. The system or population of any preceding claim, wherein the method is for
    (a) enhancing immune checkpoint antagonism or agonism therapy of the patient, optionally wherein the therapy is antibody therapy using an antibody selected from ipilimumab (or YERVOY™), tremelimumab, nivolumab (or OPDIVO™), pembrolizumab (or KEYTRUDA™), pidilizumab, BMS-936559, durvalumab and atezolizumab; or
    (b) modulating a vaccine therapy of the disease or condition; or
    (c) modulating a cell therapy (eg, adoptive immune cell therapy) of the disease or condition, optionally for dampening down the cell based therapy or a side effect thereof (eg, cytokine release syndrome); or
    (d) modulating CAR-T or TILs therapy for the treatment of a cancer in the patient; or
    (e) reducing autotoxicity in the patient mediated by T_H2 cell cytokine release.
16. The system or population of any preceding claim, wherein the disease or condition is a cancer, autoimmune disease or condition, inflammatory disease or condition, viral infection (eg, HIV infection of a human patient), an allergic disease or condition, or a disease or condition mediated or caused by a viral infection.
17. The system or population of any one of claims 2 to 16, wherein first cell population growth is reduced by at least 5-fold.
18. The system of any one of claims 2 to 5 and 7 to 17, wherein the microbiota is a gut microbiota of the patient.
19. The system or population of any preceding claim, for carrying out the method to alter the microbiota thereby stimulating Paneth cells in the patient, whereby immune cells are modulated and the disease or condition is treated or reduced.

20. A guided nuclease, for use in the system recited in any preceding claim for carrying out the method according to said claim; or a HM-CRISPR/Cas system, gRNA, HM-array or HM-crRNA for administration to a patient for therapy of a disease or condition in the patient using the method according to any preceding claim; or a HM-array, gRNA or HM-crRNA for use in a HM-CRISPR/Cas system of any preceding claim for carrying out the method according to said claim; or a vector, eg, a bacteriophage, conjugative plasmid or transposon capable of infecting or transforming a first cell, comprising or encoding the system, HM-array, gRNA or HM-crRNA; or a medicament comprising or encoding the system, HM-array, gRNA or HM-crRNA; optionally wherein the gRNA is a single guide RNA.
21. A method of treating or reducing a disease or condition in a patient, wherein the method is as recited in any one of claims 1 to 19.