

CLAIMS

1. A method of selectively modifying a selected cell population of hematopoietic origin comprising:
 - (a) forming selected cell-targeted synthetic nanocarriers by
 - (i) adding polyglutamic acid (PGA) conjugated to selected cell targeting ligands that bind the selected cell population of hematopoietic origin to a solution comprising nucleic acid encapsulated within a positively-charged carrier comprising poly(β -amino ester); and
 - (ii) incubating the solution wherein selected cell-targeted synthetic nanocarriers form within 5 minutes of the adding and comprise
 - (A) nucleic acid encapsulated within the positively-charged carrier comprising poly(β -amino ester);
 - (B) a neutrally or negatively-charged coating comprising about a 15 kDa PGA on the outer surface of the positively-charged carrier; and
 - (C) the selected cell targeting ligands extending from the outer surface of the neutrally or negatively-charged coating and conjugated to PGA within the neutrally or negatively-charged coating; and
 - (b) administering the formed selected cell-targeted synthetic nanocarriers to a heterogenous mixture of ex vivo cells comprising the selected cell population of hematopoietic origin within a serum-free media thereby selectively modifying the selected cell population of hematopoietic origin.
2. A method of claim 1 wherein the nucleic acid encodes a megaTAL of SEQ ID NO: 1 or a humanized chimeric antigen receptor of SEQ ID NO: 37.
3. A method of claim 1 wherein the nucleic acid is synthetic mRNA.
4. A method of claim 3 wherein the synthetic mRNA encodes a gene editing agent selected from transcription activator-like effector nucleases (TALENs); megaTALs; and/or zinc finger nucleases.
5. A method of claim 3 wherein the synthetic mRNA encodes a phenotype-altering protein selected from FOXO1, LKB1, TCF7, EOMES, ID2, TERT, CCR2b, and/or CCR4.

6. A method of claim 1 wherein the selected cell population of hematopoietic origin is selected from T cells, natural killer cells, monocytes, macrophages, dendritic cells, B cells, or hematopoietic stem cells.
7. A method of claim 1 wherein the selected cell targeting ligand comprises a CD4 binding domain or a CD8 binding domain.
8. A method of claim 1 wherein no cell selection or purification processes that increase the percentage of the selected cell population relative to other cells within the heterogenous mixture are performed prior to the administering.