

CLAIMS

1. A nucleic acid construct encoding a modified genome or RNA replicon of an alphavirus species, wherein at least one nonstructural protein (nsP), or a portion thereof, of the modified alphavirus genome or RNA replicon is heterologous relative to the remainder of the modified alphavirus genome or RNA replicon.
2. The nucleic acid construct of claim 1, wherein the at least one heterologous nsP or portion thereof is nsP1, nsP2, nsP3, nsP4, or a portion of any thereof, or a combination of any of the foregoing.
3. The nucleic acid construct of any one of claims 1 to 2, wherein the modified alphavirus genome or RNA replicon is devoid of at least a portion of the nucleic acid sequence encoding one or more viral structural proteins.
4. The nucleic acid construct of any one of claims 1-3, further comprising one or more expression cassettes, wherein each of the expression cassettes comprises a promoter operably linked to a heterologous nucleic acid sequence.
5. The nucleic acid construct of claim 4, wherein at least one of the expression cassettes comprises a subgenomic (*sg*) promoter operably linked to a heterologous nucleic acid sequence.
6. The nucleic acid construct of any one of claims 4-5, wherein at least one of expression cassettes comprises a coding sequence for a gene of interest (GOI).
7. The nucleic acid construct of any one of claims 1-6, wherein the nucleic acid construct is incorporated into a vector.
8. A recombinant cell comprising a nucleic acid construct according to any one of claims 1-7.
9. A cell culture comprising at least one recombinant cell according to claim 8, and a culture medium.
10. A method for functionalizing/engineering an alphavirus genome or RNA replicon, comprising:

- (a) providing a non-functional alphavirus genome or RNA replicon;
 - (b) replacing a nonstructural protein (nsP), or a portion thereof, of the non-functional alphavirus genome or RNA replicon with a heterologous coding sequence for the corresponding nsP or portion thereof derived from a different alphavirus strain to generate a modified alphavirus genome or RNA replicon;
 - (c) assessing functionality of the modified alphavirus genome or RNA replicon;
 - (d) identifying the modified alphavirus genome or RNA replicon as being functional if the modified alphavirus genome or RNA replicon is capable of RNA replication and/or expression.
11. The method of claim 10, wherein the non-functionality of the alphavirus genome or RNA replicon is determined by a deficiency in self-replication within a host cell.
12. The method of any one of claims 10-11, the assessing functionality of the modified alphavirus genome or RNA replicon comprises an assay selected from the group consisting of: detection of RNA replication, detection of viral protein expression, detection of cytopathic effect (CPE), and detection of heterologous transgene expression.
13. A transgenic animal comprising a nucleic acid construct according to any one of claims 1-7.
14. A method for producing a polypeptide of interest, comprising (i) rearing a transgenic non-human animal according to claim 13, or (ii) culturing a recombinant cell comprising a nucleic acid construct according to any one of claims 1-7 under conditions wherein the transgenic non-human animal or the recombinant cell produces the polypeptide encoded by the GOI.
15. A method for producing a polypeptide of interest in a non-human subject, comprising a nucleic acid construct according to any one of claims 6-7 to be introduced into the subject.
16. A recombinant polypeptide produced by the method of claim 15.
17. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and:
- (a) a nucleic acid construct of any one of claims 1-7;

- (b) a recombinant cell of claim 8; and/or
 - (c) a recombinant polypeptide of claim 16.
18. Use of a composition in the manufacturing of a medicament for the induction of a pharmacodynamic effect, for preventing and/or treating a health condition in a subject in need thereof, wherein composition comprises:
- (a) a nucleic acid construct of any one of claims 1-7;
 - (b) a recombinant cell of claim 8;
 - (c) a recombinant polypeptide of claim 16; and/or
 - (d) a pharmaceutical composition of claim 17,
- wherein the health condition is a proliferative disorder, inflammatory disorder, autoimmune disorder, or a microbial infection.
19. Use of a composition for inducing a pharmacodynamic effect, preventing and/or treating a health condition in a subject in need thereof, wherein the composition comprises:
- (a) a nucleic acid construct of any one of claims 1-7;
 - (b) a recombinant cell of claim 8;
 - (c) a recombinant polypeptide of claim 16; and/or
 - (d) a pharmaceutical composition of claim 17,
- wherein the health condition is a proliferative disorder, inflammatory disorder, autoimmune disorder, or a microbial infection.
20. The use of any one of claims 18-19, wherein the health condition is a rabies infection.
21. A kit for inducing a pharmacodynamic effect, for eliciting an immune response, for the prevention, and/or for the treatment of a health condition or a microbial infection, the kit comprising:
- (a) a nucleic acid construct of any one of claims 1-7;
 - (b) a recombinant cell of claim 8;
 - (c) a recombinant polypeptide of claim 16; and/or
 - (d) a pharmaceutical composition of claim 17.