Claims:

1. A conjugate delivery system composition for delivering an RNA interference polynucleotide to a liver cell *in vivo* comprising:

   RNAi-A + Melittin-(L-Gal)$_x$

   wherein,

   Melittin is a melittin peptide

   L is physiologically labile linkage,

   Gal is an Asialoglycoprotein Receptor (ASGPr) ligand,

   x is an integer having a value greater than 80% of primary amines of **Melittin**,

   RNAi is an RNA interference polynucleotide, and

   A is either a hydrophobic group having at least 20 carbon atoms or a galactose cluster.
2. The composition of claim 1 wherein the RNA interference polynucleotide is selected from the groups consisting of: DNA, RNA, dsRNA, siRNA, and microRNA.
3. The composition of claim 1 wherein the liver cell consists of a hepatocyte.
4. The composition of claim 1 wherein the ASGPr ligands are reversibly linked to at least 90% of the amines on a plurality of melittin peptides.
5. The composition of claim 1 wherein the Melittin peptide is selected from the list consisting of: Seq. ID 1, Seq. ID 7, Seq. ID 11, Seq. ID 51, Seq. ID 57, Seq. ID 58, Seq. ID 92, and Seq. ID 96.
6. The composition of claim 1 wherein the Melittin peptide consists of D-form amino acids.
7. The composition of claim 1 wherein **L** is a disubstituted maleamate.
8. The composition of claim 1 wherein **L** is a amidobenzyl carbamate.
9. The composition of claim 7 further comprising a polyethyleneglycol (PEG) covalently linked to the amino terminus of the melittin peptide.
10. The composition of claim 7 further comprising an ASGPr ligand-PEG conjugate covalently linked to the amino terminus of the melittin peptide.
11. The composition of claim 8 further comprising a polyethyleneglycol (PEG) covalently linked to the amino terminus of the melittin peptide.
12. The composition of claim 8 further comprising an ASGPr ligand-PEG conjugate covalently linked to the amino terminus of the melittin peptide.
13. The composition of claim 1 wherein the ASGPr ligand is selected from the group consisting of lactose, galactose, N-acetylgalactosamine (GalNAc), galactosamine, N-formylgalactosamine, N-acetyl-galactosamine, N-propionylgalactosamine, N-n-butanoylgalactosamine, and N-iso-butanoyl-galactosamine.

14. The composition of 1 wherein **RNAi** is linked to **A** via a physiologically labile linkage L^2.
15. The composition of 14 wherein L^2 is orthogonal to **L**.
16. The composition of claim 1 wherein the galactose cluster consists of an N-acetylgalactosamine trimer.
17. The composition of claim 1 wherein the hydrophobic group consists of cholesterol.
18. The composition of claim 1 wherein the composition is provided in a pharmaceutically acceptable carrier or diluent.
19. A method for inhibiting expression of a gene expressed in a liver cell of a mammal comprising:
    a) forming an RNAi polynucleotide having sequence identical or nearly identical to a portion of sequence of said gene; and,
    a) injecting into a vessel in said mammal a composition of claim 1.
20. A method of manufacturing an RNA interference polynucleotide delivery composition comprising:
    a) forming a melittin peptide;
    b) forming a plurality of uncharged masking agents each comprising an ASGPr ligand covalently linked to a disbustituted maleic anhydride or a dipeptide amindobenzyl amine reactive carbonate;
    c) modifying greater than 80% of primary amines on a population of melittin peptides with the masking agents of step b,
    d) linking the RNA interference polynucleotide to a hydrophobic group having at least 20 carbon atoms or a galactose trimer;
    f) providing the RNA interference polynucleotide and the modified melittin peptide in solution suitable for administration *in vivo*.

Claims:

1. A conjugate delivery system composition for delivering an RNA interference polynucleotide to a liver cell *in vivo* comprising:

   RNAi–A and **Melittin–(L–Gal)$_x$**

   wherein,

   Melittin is a melittin peptide,

   L is physiologically labile reversible linkage wherein cleavage of **L–Gal** restores an amine on Melittin,

   Gal is an Asialoglycoprotein Receptor (ASGPr) ligand,

   x is an integer having a value greater than 80% of primary amines of **Melittin**,

   RNAi is an RNA interference polynucleotide, and

   A is either a hydrophobic group having at least 20 carbon atoms or a galactose cluster.

2. The composition of claim 1 wherein the RNA interference polynucleotide is selected from the groups consisting of: DNA, RNA, dsRNA, siRNA, and microRNA.

3. The composition of claim 1 wherein the liver cell consists of a hepatocyte.

4. The composition of claim 1 wherein the ASGPr ligands are reversibly linked to at least 90% of the amines on a plurality of melittin peptides.

5. The composition of claim 1 wherein the Melittin peptide is selected from the list consisting of: Seq. ID 1, Seq. ID 7, Seq. ID 11, Seq. ID 51, Seq. ID 57, Seq. ID 58, Seq. ID 92, and Seq. ID 96.

6. The composition of claim 1 wherein the Melittin peptide consists of D-form amino acids.

7. The composition of claim 1 wherein **L** is a disubstituted maleamate.

8. The composition of claim 1 wherein **L** is a amidobenzyl carbamate.

9. The composition of claim 7 further comprising a polyethyleneglycol (PEG) covalently linked to the amino terminus of the melittin peptide.

10. The composition of claim 7 further comprising an ASGPr ligand-PEG conjugate covalently linked to the amino terminus of the melittin peptide.

11. The composition of claim 8 further comprising a polyethyleneglycol (PEG) covalently linked to the amino terminus of the melittin peptide.

12. The composition of claim 8 further comprising an ASGPr ligand-PEG conjugate covalently linked to the amino terminus of the melittin peptide.

13. The composition of claim 1 wherein the ASGPr ligand is selected from the group consisting of lactose, galactose, N-acetylgalactosamine (GalNAc), galactosamine, N-formylgalactosamine, N-propionylgalactosamine, N-n-butanoylgalactosamine, and N-iso-butanoyl-galactosamine.

14. The composition of 1 wherein **RNAi** is linked to **A** via a physiologically labile linkage $\mathbf{L}^2$.

15. The composition of 14 wherein $\mathbf{L}^2$ is orthogonal to **L**.

16. The composition of claim 1 wherein the galactose cluster consists of an N-acetylgalactosamine trimer.

17. The composition of claim 1 wherein the hydrophobic group consists of cholesterol.

18. The composition of claim 1 wherein the composition is provided in a pharmaceutically acceptable carrier or diluent.