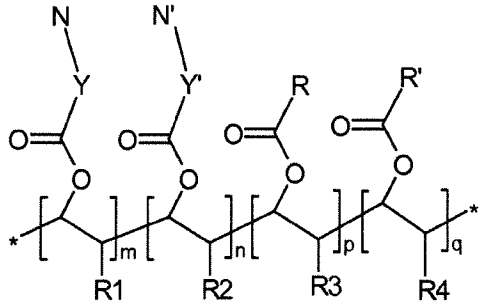
CLAIMS:

1. A poly(vinyl ester) random copolymer having the structure:



wherein:

N is $-NH_2$ or $-N-CO-O-C-(CH_3)_3$,

N' is $-NR^5H$, $-NR^5R^6$, $-NR^5R^6R^7$, nitrogen heterocycle, aldimine, hydrazide, hydrazone, or imidazole, wherein R^5, R^6, and R^7 are independently selected from $-CH_3$ and $-CH_2-CH_3$,

Y and Y' are independently $-(CH_2)_a-$ or $-(CH_2-CH_2-O)_b-(CH_2)_c-$ wherein *a* , *b*, and *c* are independently 1, 2, 3, 4, 5, or 6,

R is a hydrophobic group having 1-7 carbon atoms or an alkoxy ethyl group,

R' is a hydrophobic group having 12-20 carbon atoms,

R1, R2, R3, and R4 are independently selected from hydrogen (−H) and methyl ($-CH_3$),

m and p are independently integers greater than zero (0),

n and q are independently integers greater than or equal to zero (0), and

the ratio (m+n)/(p+q) is 1-9.

2. The poly(vinyl ester) random copolymer of claim 1 wherein the ratio (m+n)/(p+q) is 1.5-4.

3. The poly(vinyl ester) random copolymer of claim 1 wherein the polydispersity of the polymer is less than 1.5

4. The poly(vinyl ester) random copolymer of claim 1 wherein Y is $-(CH_2)_a-$ wherein *a* is 2, 3, or 4.

5. The poly(vinyl ester) random copolymer of claim 1 wherein Y is $-CH_2-CH_2-O-CH_2-CH_2-$.

6. The poly(vinyl ester) random copolymer of claim 1 wherein R is $-(CH_2)_k-CH_3$ wherein *k* is 1, 2, 3, 4, or 6.

7. The poly(vinyl ester) random copolymer of claim 1 wherein n is zero.

8. The poly(vinyl ester) random copolymer of claim 7 wherein q is zero.
9. The poly(vinyl ester) random copolymer of claim 1 wherein R1, R2, R3 and R4 are each hydrogen.
10. The poly(vinyl ester) random copolymer of claim 1 wherein:

    Y is $-(CH_2)_4-$

    R is $-(CH_2)_2-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.
11. The poly(vinyl ester) random copolymer of claim 10 wherein ratio m/p is 1.3-2.3.
12. The poly(vinyl ester) random copolymer of claim 1 wherein:

    Y is $-(CH_2)_2-$

    R is $-(CH_2)_2-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.
13. The poly(vinyl ester) random copolymer of claim 1 wherein:

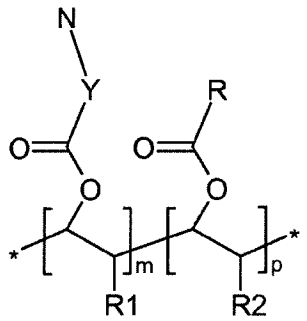
    Y is $-(CH_2)_2-$

    R is $-(CH_2)_3-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.
14. The poly(vinyl ester) random copolymer of claim 1 wherein the polymer is conjugated to an RNA interference polynucleotide.
15. The poly(vinyl ester) random copolymer of claim 1 wherein greater than 50% of N are reversibly modified by reaction with disubstituted maleic anhydride masking agents, dipeptide-amidobenzyl-carbonate masking agents, or a combination of disubstituted maleic anhydride masking agents and dipeptide-amidobenzyl-carbonate masking agents.
16. A composition for inhibiting gene expression in vivo comprising the poly(acrylate) random copolymer of claim 16 and an RNA interference polynucleotide in a pharmaceutically acceptable carrier.
17. The composition of claim 16 wherein the RNA interference polynucleotide is covalently linked to the poly(vinyl ester) random copolymer.
18. The composition of claim 16 wherein the RNA interference polynucleotide is conjugated to a hydrophobic group containing at least 20 carbon atoms.

19. A poly(vinyl ester) random copolymer having the structure:



wherein:

N is a primary amine having the form $-NH_2$,

Y is $-(CH_2)_a-$ or $-(CH_2-CH_2-O)_b-(CH_2)_c-$ wherein *a* , *b*, and *c* are independently 1, 2, 3, 4, 5, or 6,

R is a hydrophobic group having 1-7 carbon atoms,

R1 and R2 are independently selected from hydrogen (−H) and methyl ($-CH_3$),

m is an integer greater than zero (0),

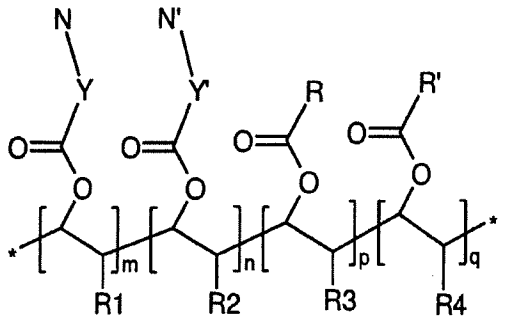
p is an integer greater than zero (0), and

the ratio m/p is 1-9.

20. The poly(vinyl ester) random copolymer of claim 19 wherein the ratio m/p is 1.5-4.

CLAIMS:

1. A membrane active poly(vinyl ester) random copolymer having the structure represented by:



wherein:

N is $-NH_2$ or $-N-CO-O-C-(CH_3)_3$,

N' is $-NR^5H$, $-NR^5R^6$, $-NR^5R^6R^7$, nitrogen heterocycle, aldimine, hydrazide, hydrazone, or imidazole, wherein R^5, R^6, and R^7 are independently selected from $-CH_3$ and $-CH_2-CH_3$,

Y and Y' are independently $-(CH_2)_a-$ or $-(CH_2-CH_2-O)_b-(CH_2)_c-$ wherein a , b, and c are independently 1, 2, 3, 4, 5, or 6,

R is a hydrophobic group having 1-7 carbon atoms or an alkoxy ethyl group,

R' is a hydrophobic group having 12-20 carbon atoms,

R1, R2, R3, and R4 are independently selected from hydrogen (−H) and methyl ($-CH_3$),

m and p are independently integers greater than zero (0),

n and q are independently integers greater than or equal to zero (0),

the ratio (m+n)/(p+q) is 1-9, and

the poly(vinyl ester) random copolymer is capable of lysing red blood cells.

2. The poly(vinyl ester) random copolymer of claim 1 wherein the ratio (m+n)/(p+q) is 1.5-4.
3. The poly(vinyl ester) random copolymer of claim 1 wherein the polydispersity of the polymer is less than 1.5
4. The poly(vinyl ester) random copolymer of claim 1 wherein Y is $-(CH_2)_a-$ wherein a is 2, 3, or 4.
5. The poly(vinyl ester) random copolymer of claim 1 wherein Y is $-CH_2-CH_2-O-CH_2-CH_2-$.

6. The poly(vinyl ester) random copolymer of claim 1 wherein R is $-(CH_2)_k-CH_3$ wherein k is 1, 2, 3, 4, or 6.

7. The poly(vinyl ester) random copolymer of claim 1 wherein n is zero.

8. The poly(vinyl ester) random copolymer of claim 7 wherein q is zero.

9. The poly(vinyl ester) random copolymer of claim 1 wherein R1, R2, R3 and R4 are each hydrogen.

10. The poly(vinyl ester) random copolymer of claim 1 wherein:

    Y is $-(CH_2)_4-$

    R is $-(CH_2)_2-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.

11. The poly(vinyl ester) random copolymer of claim 10 wherein ratio m/p is 1.3-2.3.

12. The poly(vinyl ester) random copolymer of claim 1 wherein:

    Y is $-(CH_2)_2-$

    R is $-(CH_2)_2-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.

13. The poly(vinyl ester) random copolymer of claim 1 wherein:

    Y is $-(CH_2)_2-$

    R is $-(CH_2)_3-CH_3$

    R1 and R3 are each hydrogen, and

    n and p are each zero.

14. The poly(vinyl ester) random copolymer of claim 1 wherein the polymer is conjugated to an RNA interference polynucleotide.

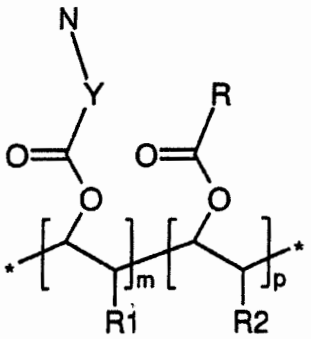
15. The poly(vinyl ester) random copolymer of claim 1 wherein greater than 50% of N are reversibly modified by reaction with disubstituted maleic anhydride masking agents, dipeptide-amidobenzyl-carbonate masking agents, or a combination of disubstituted maleic anhydride masking agents and dipeptide-amidobenzyl-carbonate masking agents.

16. A composition for inhibiting gene expression in vivo comprising the poly(vinyl ester) random copolymer of claim 1 and an RNA interference polynucleotide in a pharmaceutically acceptable carrier.

17. The composition of claim 16 wherein the RNA interference polynucleotide is covalently linked to the poly(vinyl ester) random copolymer.

18. The composition of claim 16 wherein the RNA interference polynucleotide is conjugated to a hydrophobic group containing at least 20 carbon atoms.

19. A membrane active poly(vinyl ester) random copolymer having the structure represented by:



wherein:

N is a primary amine having the form $-NH_2$,

Y is $-(CH_2)_a-$ or $-(CH_2-CH_2-O)_b-(CH_2)_c-$ wherein a , b, and c are independently 1, 2, 3, 4, 5, or 6,

R is a hydrophobic group having 1-7 carbon atoms,

R1 and R2 are independently selected from hydrogen (−H) and methyl ($-CH_3$),

m is an integer greater than zero (0),

p is an integer greater than zero (0),

the ratio m/p is 1-9, and

the poly(vinyl ester) random copolymer is capable of lysing red blood cells.

20. The poly(vinyl ester) random copolymer of claim 19 wherein the ratio m/p is 1.5-4.

21. The poly(vinyl ester) random copolymer of claim 19 wherein a is 1, 2, or 3, b is 1, c is 2, R1 and R2 are hydrogen, and the ratio m/p is 1-4.

22. The poly(vinyl ester) random copolymer of claim 21 wherein the polydispersity is less than or equal to 1.5.

23. The poly(vinyl ester) random copolymer of claim 22 wherein the polydispersity of the polymer is less than or equal to 1.3.
24. The poly(vinyl ester) random copolymer of claim 22 wherein the ratio m/n is about 1.
25. The poly(vinyl ester) random copolymer of claim 22 wherein the ratio m/n is about 3.
26. The poly(vinyl ester) random copolymer of any of claims 21-25 wherein Y is (CH_2).
27. The poly(vinyl ester) random copolymer of any of claims 21-25 wherein Y is $(CH_2)_2$.
28. The poly(vinyl ester) random copolymer of any of claims 21-25 wherein Y is $(CH_2)_3$.
29. The poly(vinyl ester) random copolymer of any of claims 21-25 wherein Y is $(CH_2)_2$–O–$(CH_2)_2$.
30. The poly(vinyl ester) random copolymer of any of claims 21-29 wherein R is a hydrophobic group having 3 carbon atoms.
31. The poly(vinyl ester) random copolymer of any of claims 21-29 wherein R is a hydrophobic group having 4 carbon atoms.
32. The poly(vinyl ester) random copolymer of any of claims 30-31 wherein the hydrophobic group is branched.
33. The poly(vinyl ester) random copolymer of any of claims 21-32 wherein greater than 50% of N are reversibly modified by reaction with disubstituted maleic anhydride masking agents, dipeptide-amidobenzyl-carbonate masking agents, or a combination of disubstituted maleic anhydride masking agents and dipeptide-amidobenzyl-carbonate masking agents.
34. The poly(vinyl ester) random copolymer of claim 33 wherein the polymer is conjugated to an RNA interference polynucleotide.
35. A composition for inhibiting gene expression in vivo comprising the poly(vinyl ester) random copolymer of claim 33 and an RNA interference polynucleotide in a pharmaceutically acceptable carrier.
36. The composition of claim 35 wherein the poly(vinyl ester) random copolymer is conjugated to an RNA interference polynucleotide.
37. The composition of claim 35 wherein the RNA interference polynucleotide is conjugated to a hydrophobic group containing at least 20 carbon atoms.