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(71) Applicant (for all designated States except US): **ARROW-HEAD RESEARCH CORPORATION** [US/US]; 225 South Lake Avenue, 3rd Floor, Pasadena, CA 91101 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ROZEMA, David, B.** [US/US]; 9418 Whippoorwill Way, Middleton, WI 53562 (US). **LEWIS, David, L.** [US/US]; 505 Maple Avenue, Madison, WI 53706 (US). **WAKEFIELD, Darren,**

H. [US/US]; 3168 Stoneman Drive, Fitchburg, WI 53711 (US). **KITAS, Eric** [AU/CH]; Elchbergweg 4, CH-4147 Aesch, Baselland (CH). **HADWIGER, Philipp** [AT/DE]; Heinrich-Hoffman-Strasse 17, 95326 Kulmbach (DE). **WOLFF, Jon, A.** [US/US]; 3506 Lake Mendota Drive, Madison, WI 53705 (US). **ROEHL, Ingo** [DE/DE]; Bergaecker 8, 96117 Memmelsdorf (DE). **MOHR, Peter** [CH/CH]; Benkenstrasse 26, CH-4054 Basel (CH). **HOFFMAN, Torsten** [DE/DE]; Kleinhueningerstrasse 15, 79576 Weil am Rhein (DE). **JAHN-HOFMANN, Kerstin** [DE/DE]; Stoltzestr 39, 63263 Neu-Isenburg (DE). **MUELLER, Hans, Martin** [DE/DE]; Westendstrasse 30, 80339 Munich (DE). **OTT, Guenther** [DE/DE]; Munckerstr. 32, 95444 Bayreuth (DE). **BLOKHIN, Andrei, V.** [US/US]; 5770 Dawley Drive, Fitchburg, WI 53711 (US). **BENSON, Jonathan, D.** [US/US]; 701 Hoel Avenue, Stoughton, WI 53589 (US). **CARLSON, Jeffrey, C.** [US/US]; 303 N. Hamilton #309, Madison, WI 53703 (US).

(74) Agent: **MILLS, Jeffrey, K.**; Fanelli Haag PLLC, 1909 K Street, N.W., Suite 1120, Washington, DC 20006 (US).

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[Continued on next page]

(54) Title: PEPTIDE-BASED IN VIVO SIRNA DELIVERY SYSTEM

FIG. 1. Melittin peptide sequences.

Seq ID	Melittin Sequence	Name
1	GIQAILKVLATGLPTLISWIKNRKQ	App. 1000
2	GIQAILKVLATGLPTLISWIKNRKQ	G1A
3	GIQAILKVLATGLPTLISWIKNRKQ	G1C
4	GIQAILKVLATGLPTLISWIKNRKQ	G1F
5	GIQAILKVLATGLPTLISWIKNRKQ	G1H
6	GIQAILKVLATGLPTLISWIKNRKQ	G1J
7	GIQAILKVLATGLPTLISWIKNRKQ	G1L
8	GIQAILKVLATGLPTLISWIKNRKQ	G1M
9	GIQAILKVLATGLPTLISWIKNRKQ	G1Y
10	GIQAILKVLATGLPTLISWIKNRKQ	G1W
11	GIQAILKVLATGLPTLISWIKNRKQ	G1Y
12	GIQAILKVLATGLPTLISWIKNRKQ	T11C dM1
13	GIQAILKVLATGLPTLISWIKNRKQ	G12L
14	GIQAILKVLATGLPTLISWIKNRKQ	G12W
15	GIQAILKVLATGLPTLISWIKNRKQ	K22T
16	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K7N
17	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K7A
18	GIQAILKVLATGLPTLISWIKNRKQ	G1L, K7D
19	GIQAILKVLATGLPTLISWIKNRKQ	G1L, K7R
20	GIQAILKVLATGLPTLISWIKNRKQ	G1L, K7H
21	GIQAILKVLATGLPTLISWIKNRKQ	G1L, T11C
22	GIQAILKVLATGLPTLISWIKNRKQ	G1L, G12L
23	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, P14L
24	GIQAILKVLATGLPTLISWIKNRKQ	G1L, T13C
25	GIQAILKVLATGLPTLISWIKNRKQ	G1L, S18C
26	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, W19A
27	GIQAILKVLATGLPTLISWIKNRKQ	T11C, I20L
28	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K21A
29	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K23A
30	GIQAILKVLATGLPTLISWIKNRKQ	G1L, B24A
31	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K25A
32	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, Q26C
33	GIQAILKVLATGLPTLISWIKNRKQ	G1L, T11C
34	GIQAILKVLATGLPTLISWIKNRKQ	G1L, I21C
35	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K27A, K21A
36	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K27A, K23A
37	GIQAILKVLATGLPTLISWIKNRKQ	G1L, T11C, I17L
38	GIQAILKVLATGLPTLISWIKNRKQ	G1L, T11C, S18C
39	GIQAILKVLATGLPTLISWIKNRKQ	T11G, T15G, S18C
40	GIQAILKVLATGLPTLISWIKNRKQ	T11A, T15A, S18A
41	GIQAILKVLATGLPTLISWIKNRKQ	G1Y, K27A, K21A, K23A

FIG. 1

(57) Abstract: The present invention is directed compositions for targeted delivery of RNA interference (RNAi) polynucleotides to hepatocytes *in vivo*. Targeted RNAi polynucleotides are administered together with co-targeted melittin delivery peptides. Delivery peptides provide membrane penetration function for movement of the RNAi polynucleotides from outside the cell to inside the cell. Reversible modification provides physiological responsiveness to the delivery peptides.



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