**Supplementary Materials**

**Design, Synthesis, and Evaluation of Oleyl-WRH Peptides for siRNA Delivery**

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**Figure S1.** (WRH)1: MALDI-TOF (m/z) C23H33N9O4 Calculated: 499.2645, Found: 499.4015 [M+2H]+.



**Figure S2.** (WRH)2: MALDI-TOF (m/z) C46H62N18O7 Calculated: 978.5038, Found: 978.4187 [M+2H]+.



**Figure S3.** (WRH)3: MALDI-TOF (m/z) C69H90N27O10 Calculated: 1456.7358, Found: 1456.5664 [M+H]+.



**Figure S4.** (WRH)4: MALDI-TOF (m/z) C92H119N36O13 Calculated: 1935.9752, Found: 1935.6767 [M+H]+.



**Figure S5.** Oleyl-(WRH)1: MALDI-TOF (m/z) C41H65N9O5 Calculated: 763.5098, Found: 763.6974 [M+2H]+.



**Figure S6.** Oleyl-(WRH)2: MALDI-TOF (m/z) C64H94N18O8 Calculated: 1242.7491, Found: 1242.9278 [M+2H]+.



**Figure S7.** Oleyl-(WRH)3: MALDI-TOF (m/z) C87H122N27O11 Calculated: 1720.9812, Found: 1720.6871 [M+H]+.



**Figure S8.** Oleyl-(WRH)4: MALDI-TOF (m/z) C112H152N36O14 Calculated: 2201.2278, Found: 2201.7647 [M+2H]+.

**Analytical HPLC Purification Analysis**

The purity of the most efficient peptides (WRH)3, (WRH)4, oleyl-(WRH)3, and oleyl- (WRH)4 was determined using the reverse phase analytical HPLC method at a flow rate of 0.4 mL/min on Shimadzu (LC-20ADXR) with a gradient system of water with 0.1% Formic Acid (solvent A) and acetonitrile with 0.1% Formic Acid (solvent B), using (Phenomenex Luna, 4 um C18 150 × 4.6 mm HPLC Column).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Time** | 0.01 | 5.0 | 15.0 | 25.0 | 28.0 | 33.0 | 33.0 | 38.0 |
| **% Solvent B** | 5 | 5 | 20 | 70 | 95 | 95 | 5 | 5 |

### **HPLC Chromatograms**



**Figure S9.** Analytical HPLC chromatogram of (WRH)3

|  |  |
| --- | --- |
| **Peptide** | (WRH)3 |
| **Pump A** | 0.1% Formic Acid in 100% Water |
| **Pump B** | 0.1% Formic Acid in 100% Acetonitrile |
| **Total Flow** | 0.4 ml/min |
| **Retention Time** | 22.789 min |
| **% Purity** | 95.741 |



**Figure S10.** Analytical HPLC chromatogram of (WRH)4.

|  |  |
| --- | --- |
| **Peptide** | (WRH)4 |
| **Pump A** | 0.1% Formic Acid in 100% Water |
| **Pump B** | 0.1% Formic Acid in 100% Acetonitrile |
| **Total Flow** | 0.4 ml/min |
| **Retention Time** | 21.640 min |
| **% Purity** | 96.495 |



**Figure S11.** Analytical HPLC chromatogram of Oleyl-(WRH)3.

|  |  |
| --- | --- |
| **Peptide** | Oleyl-(WRH)3 |
| **Pump A** | 0.1% Formic Acid in 100% Water |
| **Pump B** | 0.1% Formic Acid in 100% Acetonitrile |
| **Total Flow** | 0.4 ml/min |
| **Retention Time** | 21.729 min |
| **% Purity** | 97.318 |



**Figure S12.** Analytical HPLC chromatogram of Oleyl-(WRH)4.

|  |  |
| --- | --- |
| **Peptide** | Oleyl-(WRH)4 |
| **Pump A** | 0.1% Formic Acid in 100% Water |
| **Pump B** | 0.1% Formic Acid in 100% Acetonitrile |
| **Total Flow** | 0.4 ml/min |
| **Retention Time** | 21.288 min |
| **% Purity** | 95.359 |