# Electronic Supplementary Information (ESI)

## RGD Peptide-based Lipids for Targeted mRNA Delivery and Gene Editing Application

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**Table S1.** Physical characterization of RGD-LNPs

| LNP formulation | Diameter (nm) | Polydispersity index (PDI) | Encapsulation efficiency (%) |
|---|---|---|---|
| 1A | 63.34 | 0.238 | 36.03 |
| 1B | 75.73 | 0.036 | 21.29 |
| 1C | 57.27 | 0.189 | 8.14 |
| 1D | 77.09 | 0.043 | 41.78 |
| 1E | 86.61 | 0.171 | 42.14 |
| 2A | 82.83 | 0.270 | 48.15 |
| 2B | 51.85 | 0.270 | 19.38 |
| 2C | 64.09 | 0.078 | 6.34 |
| 2D | 68.45 | 0.130 | 2.69 |
| 2E | 224.1 | 0.109 | 1.57 |
| 3A | 52.09 | 0.176 | 3.89 |
| 3B | 46.68 | 0.174 | 6.93 |
| 3C | 82.25 | 0.165 | 3.87 |
| 3D | 109.6 | 0.219 | 6.50 |
| 3E | 100.9 | 0.165 | 2.49 |
| 4A | 95.46 | 0.297 | 3.78 |
| 4B | 75.25 | 0.057 | 2.56 |
| 4C | 58.43 | 0.088 | 2.47 |
| 4D | 108.8 | 0.574 | 4.29 |
| 4E | 93.68 | 0.076 | 5.32 |

**Table S2.** Physical characterization of RGD-LNPs with varying amounts of C12-200

| LNP formulation | Diameter (nm) | Polydispersity index (PDI) | Encapsulation efficiency (%) |
|---|---|---|---|
| C12-200 | 79.09 | 0.152 | 89.11 |
| 1A | 106.70 | 0.122 | 89.49 |
| 1B | 88.77 | 0.061 | 89.62 |
| 1C | 103.9 | 0.931 | 86.46 |
| 1D | 92.54 | 0.088 | 81.14 |
| 1E | 86.17 | 0.192 | 88.44 |
| 2A | 130.70 | 0.224 | 75.06 |
| 2B | 76.65 | 0.011 | 72.61 |

**Table S3.** Physical characterization of RGD-LNPs with the addition of C12-200

| LNP | Diameter (nm) | Polydispersity index (PDI) | Encapsulation efficiency (%) |
|---|---|---|---|
| 10% RGD-lipid + 90% C12-200 | 123.14 | 0.134 | 73.29 |
| 20% RGD-lipid + 80% C12-200 | 133.65 | 0.227 | 82.48 |
| 30% RGD-lipid + 70% C12-200 | 104.83 | 0.128 | 79.32 |
| 40% RGD-lipid + 60% C12-200 | 122.34 | 0.313 | 70.45 |
| 50% RGD-lipid + 50% C12-200 | 119.97 | 0.236 | 51.99 |

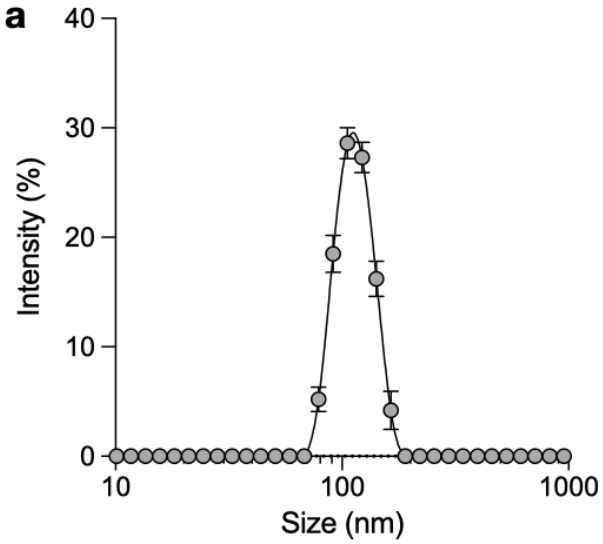


**Figure S1.** Dynamic light scattering (DLS) analysis of RGD-LNP 1A, showing the size and size distribution of n+3 measurements

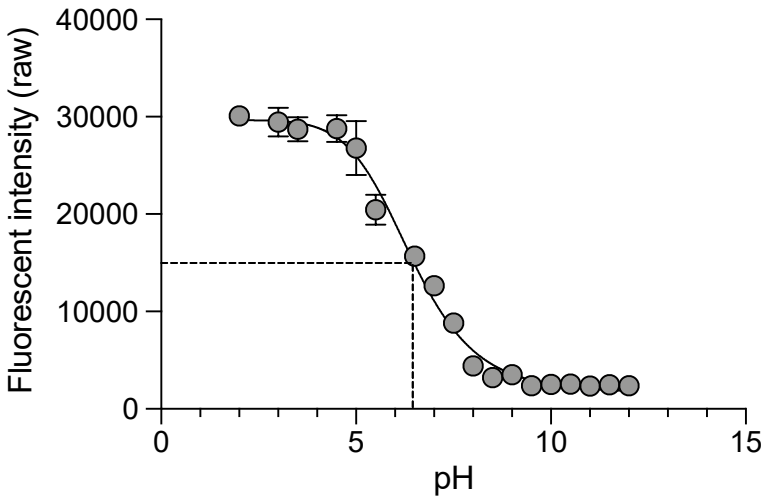


**Figure S2.** Result to determine RGD-lipid LNP (1A) pKa for the LNPs encapsulating luciferase mRNA. pKa is calculated as the pH corresponding to half of the maximum fluorescence value.

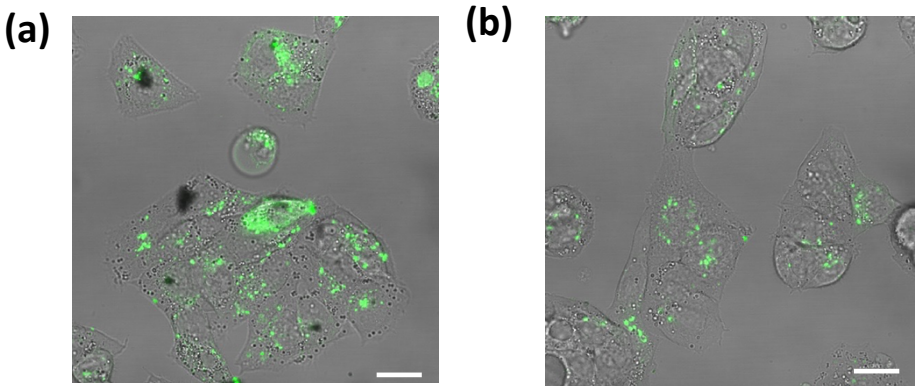


**Figure S3.** Confocal images (6h treat time with 1% DiO-labelling) to test the uptake of HepG2 cells for (A) C12-RGD hybrid LNP (lead LNP); (B) C12-200 LNP as a control. Scale bar: 20 μm.

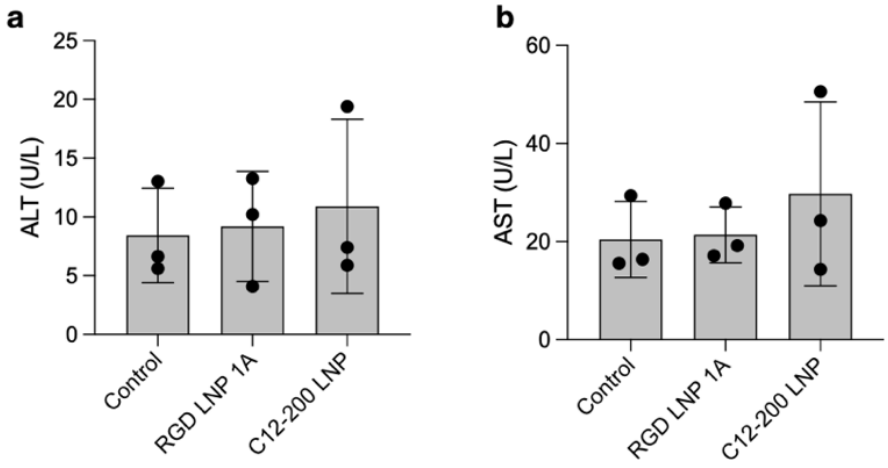


**Figure S4.** Liver enzymes for in vivo experiments indicates minimal toxicity

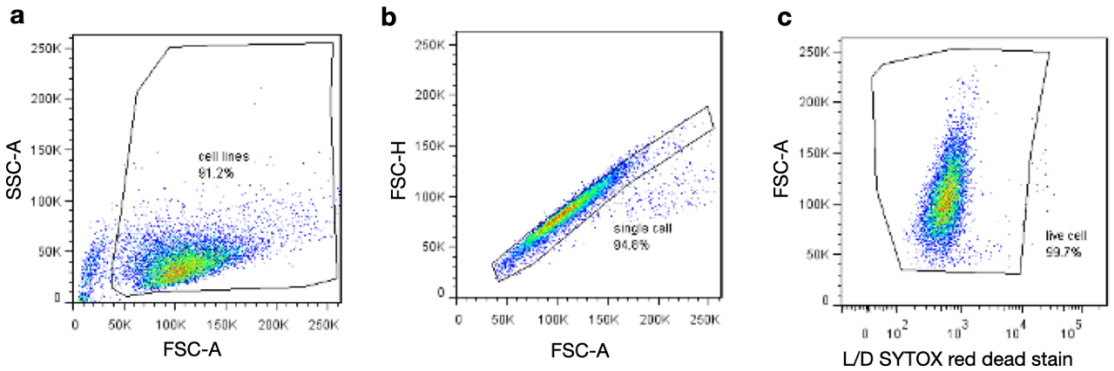


**Figure S5.** Flow gating strategy for knockdown of GFP expression in GFP+ HepG2 cells