Supporting Information

Bifunctional supramolecular nanofiber inhibits atherosclerosis by enhancing plaque stability and anti-inflammation in apoE⁻/⁻ mice

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Characteristic of compounds:

Npx-D²FGSSSR: ¹H NMR (400 MHz, DMSO-d₆) δ 8.29 (t, J = 5.5 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.12 (m, 5H), 8.01 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 8.9 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.59 (s, 2H), 7.29 (s, 5H), 7.24 – 7.20 (m, 3H), 7.16 (dd, J = 8.9, 2.3 Hz, 2H), 6.97 – 6.92 (m, 5H), 4.59 (m, 1H), 4.46 (d, J = 16.9 Hz, 3H), 4.37 (m, 3H), 4.23 – 4.18 (m, 2H), 3.88 (d, J = 5.7 Hz, 4H), 3.83 (d, J = 5.2 Hz, 2H), 3.79 (d, J = 6.9 Hz, 1H), 3.67 – 3.61 (m, 5H), 3.11 (t, J = 8.7 Hz, 3H), 2.88 (m 2H), 2.70 (dd, J = 13.5, 9.8 Hz, 1H), 1.82 – 1.72 (m, 1H), 1.65 – 1.58 (m, 1H), 1.53 (m, 2H), 1.35 (d, J = 6.9 Hz, 3H). HR-MS: calc. M = 998.4498, obsvd. (M+H)+ = 999.4559.
Figure S1. $^1$H-NMR spectrum of Npx-$^\text{D}$DFGSSSR (compound 1).

Figure S2. HR-MS spectrum of Npx-$^\text{D}$DFGSSSR (compound 1).

Npx-FFGSSSR: $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.28 – 8.18 (m, 2H), 8.15 (d, J = 7.8 Hz, 2H), 8.09 (s, 2H), 8.04 (d, J = 7.5 Hz, 1H), 7.74 (dd, J = 15.0, 8.8 Hz, 2H), 7.66 (d, J = 6.9 Hz, 2H), 7.36 (d, J = 8.2 Hz, 1H), 7.29 (s, 1H), 7.24 (s, 5H), 7.16 (d, J = 4.4 Hz, 3H), 7.10 (d, J = 6.9 Hz, 2H), 7.04 (d, J = 6.8 Hz, 1H), 4.57 (d, J = 0.5 Hz, 1H), 4.50 (d, J = 3.1 Hz, 1H), 4.41 (s, 2H), 4.37 (s, 2H), 4.23 – 4.17 (m, 1H), 3.87 (s, 4H), 3.80 (s, 3H), 3.75 (d, J = 7.2 Hz, 2H), 3.66 – 3.59 (m, 6H), 3.12 (d, J = 4.9 Hz, 2H),
3.01 (m, 2H), 2.77 (m, 2H), 1.78 (d, \(J = 6.7\) Hz, 1H), 1.64 (m, 1H), 1.52 (d, \(J = 4.7\) Hz, 2H), 1.35 (d, \(J = 6.6\) Hz, 1H), 1.21 (d, \(J = 6.5\) Hz, 3H). HR-MS: calc. M = 998.4498, obsvd. (M+H)^+ = 999.4559.

**Figure S3.** \(^1\)H-NMR spectrum of Npx-FFGSSSR (compound 2).

**Figure S4.** HR-MS spectrum of Npx-FFGSSSR (compound 2).
Nap-FFGSSSR: $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 8.26 (s, 1H), 8.13 (m, 4H), 7.96 (d, $J = 6.3$ Hz, 1H), 7.71 (d, $J = 7.8$ Hz, 1H), 7.63 (d, $J = 7.1$ Hz, 1H), 7.54 (d, $J = 20.1$ Hz, 2H), 7.18 (m, 10H), 6.93 (s, 5H), 4.39 (m, 6H), 3.93 – 3.73 (m, 7H), 3.61 (s, 18H), 3.08 (s, 3H), 2.85 (s, 2H), 2.68 (s, 1H), 1.84 – 1.41 (m, 3H), 1.33 (s, 2H). HR-MS: calc. M = 954.4236, obsvd. (M+H)$^+$ = 955.4293.

Figure S5. $^1$H-NMR spectrum of Nap-FFGSSSR (compound 3).

Figure S6. HR-MS spectrum of Nap-FFGSSSR (compound 3).
**Nap-FFGSRSS:** $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.35 (d, $J = 8.3$ Hz, 1H), 8.29 (d, $J = 6.4$ Hz, 2H), 8.22 (d, $J = 7.9$ Hz, 1H), 8.10 (d, $J = 7.2$ Hz, 1H), 8.03 (d, $J = 7.5$ Hz, 2H), 7.88 (d, $J = 7.6$ Hz, 1H), 7.81 (s, 1H), 7.79 (s, 1H), 7.78 (s, 1H), 7.76 (s, 1H), 7.59 (m, 2H), 7.53 – 7.45 (m, 2H), 7.26 (t, $J = 7.8$ Hz, 4H), 7.22 (s, 1H), 7.18 (d, $J = 7.4$ Hz, 7H), 4.63 – 4.51 (m, 3H), 4.40 (m, 4H), 4.31 – 4.26 (m, 2H), 3.83 (s, 2H), 3.75 (m, 1H), 3.66 (d, $J = 3.6$ Hz, 2H), 3.61 (m, 4H), 3.53 (s, 1H), 3.50 (s, 1H), 3.11 (d, $J = 6.1$ Hz, 2H), 3.07 (d, $J = 4.1$ Hz, 1H), 3.01 (d, $J = 4.0$ Hz, 1H), 2.98 (d, $J = 3.8$ Hz, 1H), 2.86 (m, 1H), 2.75 (m, 1H), 1.81 (d, $J = 7.8$ Hz, 1H), 1.61 (d, $J = 7.0$ Hz, 1H), 1.55 (d, $J = 7.2$ Hz, 2H). HR-MS: calc. M = 954.4236, obsvd. (M+H)$^+$ = 955.43.

**Figure S7.** $^1$H-NMR spectrum of Nap-FFGSRSS (compound 4).
**Figure S8.** HR-MS spectrum of Nap-FFGSRSS (compound 4).

**Figure S9.** Transmittance of the four hydrogels as a function of the wavelength.

**Figure S10.** Dynamic frequency sweep of hydrogel 1 (H1) at strain of 1% at 37 °C
**Figure S11.** Dynamic frequency sweep of hydrogel 2 (H2) at strain of 1% at 37 °C

**Figure S12.** Dynamic frequency sweep of hydrogel 3 (H3) at strain of 1% at 37 °C

**Figure S13.** Dynamic frequency sweep of hydrogel 4 (H4) at strain of 1% at 37 °C
**Figure S14.** Cholesterol efflux of peritoneal macrophage were assessed after treatment as indicated, n=5. Data are presented as mean ± SEM, *P < 0.05, **P < 0.01, ***P < 0.001, significantly different as indicated.

**Figure S15.** Effects of Npx and IGF-1 mimetic peptide on inflammation and cholesterol efflux. (A) qRT-PCR analysis of TNFα and IL-1β in macrophage after indicated treatment, n=5. (B) Cholesterol efflux of peritoneal macrophage were assessed after treatment as indicated, n=5. Data are presented as mean ± SEM, ***P < 0.001, ****P < 0.0001 significantly different as indicated. ns: not significantly different.