

Amphiphilic star polypept(o)ides as nanomeric vectors in mucosal drug delivery

Dimitrios Skoulas,^{‡,§} Vivien Stuettgen,^{#,§} Rachel Gaul,[§] Sally-Ann Cryan^{§,§,†} David J. Brayden,^{#,§,*} Andreas Heise^{‡,§,†,*}

[‡] Department of Chemistry, Royal College of Surgeons in Ireland, 123 St. Stephens Green, Dublin 2, Ireland. [#]School of Veterinary Medicine and Conway Institute, University College Dublin, Veterinary Science Centre, Belfield, Dublin 4, Ireland. [§]School of Pharmacy and Biomolecular Sciences and Tissue Engineering Research Group, Royal College of Surgeons in Ireland, 123 St. Stephen's Green, Dublin 2, Ireland [§]Science Foundation Ireland (SFI) Centre for Research in Medical Devices (CURAM). [†]AMBER, The SFI Advanced Materials and Bioengineering Research Centre.

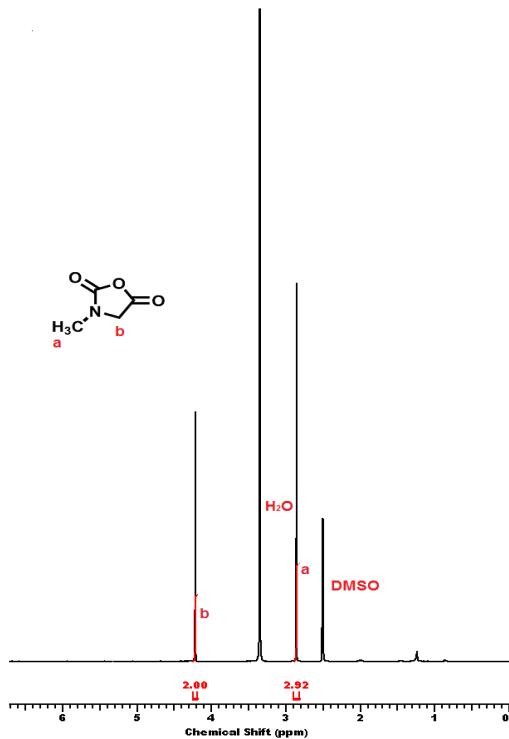


Figure S1. ¹H-NMR spectrum of Sar NCA.

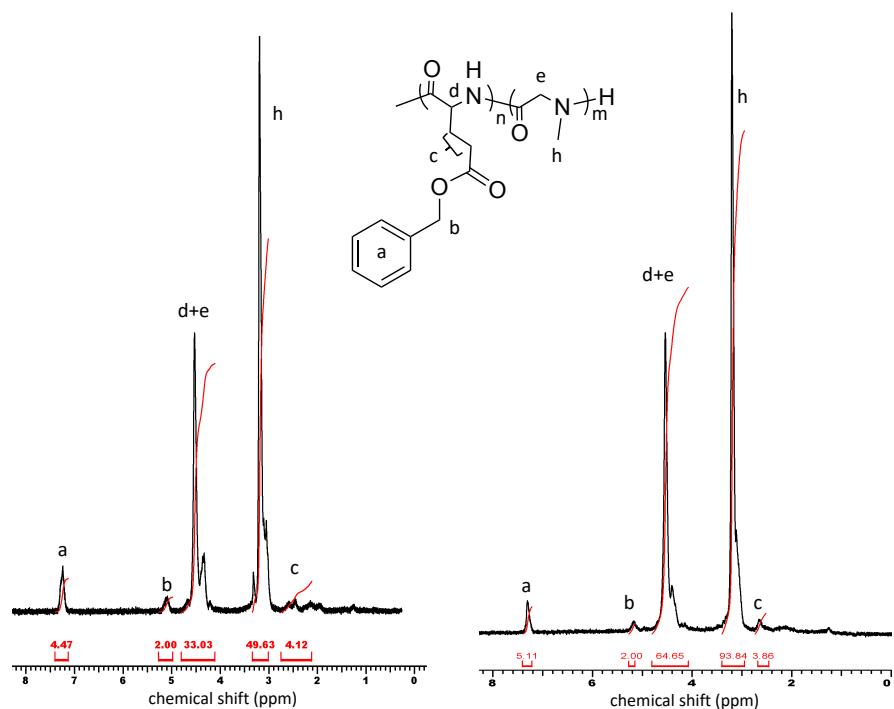


Figure S2. Representative ^1H -NMR spectra of S10 (PBLG₂₀-*b*-PSar₃₂₀), left, and S11 (PBLG₂₀-*b*-PSar₆₄₀), right, in TFA.

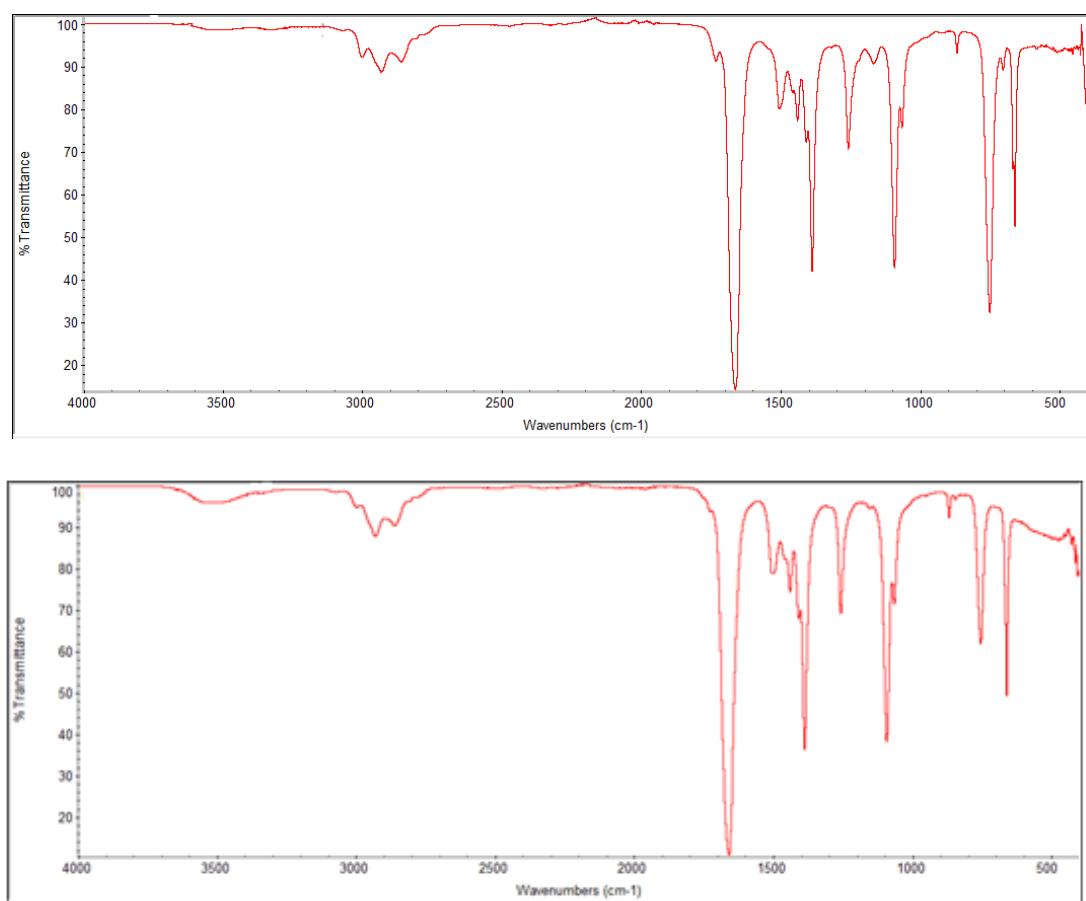


Figure S3. FTIR spectra of 8-arm starPBLG₂₀ (top) and starPBLG₂₀-*b*-PSar₆₄₀ (bottom).

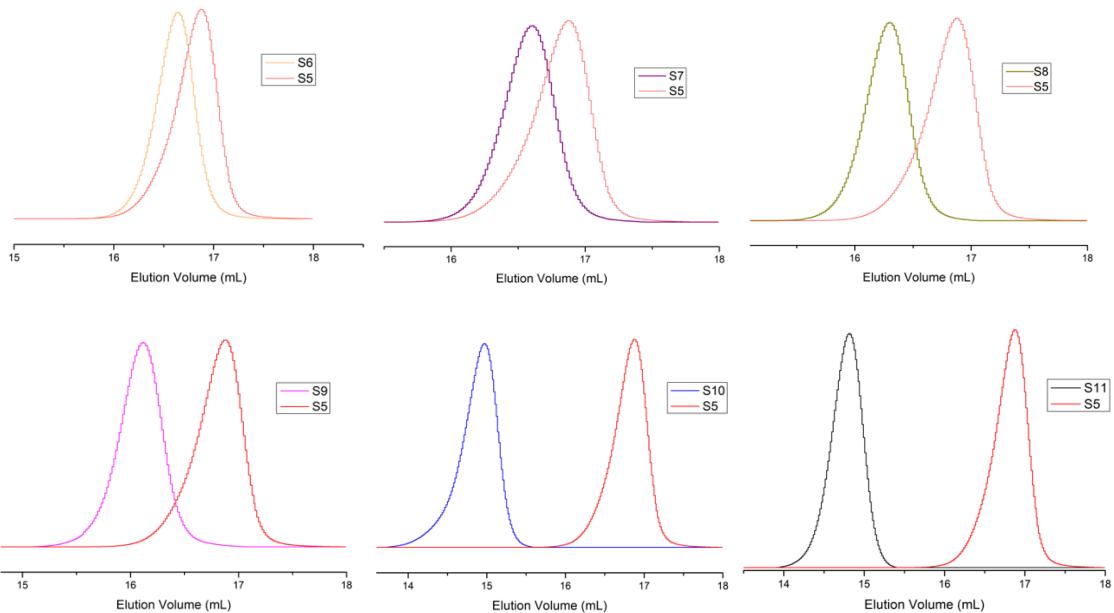


Figure S4. GPC traces of 8-arm star PBLG (S5) and polypept(o)ide star polymers S6-S11.

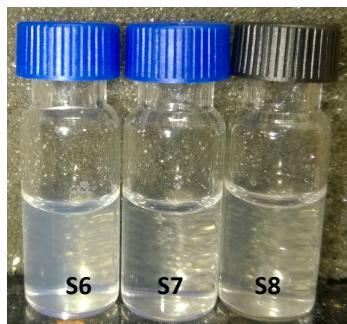


Figure S5. Solutions of star polypept(o)ides S6-S8 in water (5 mg/mL)

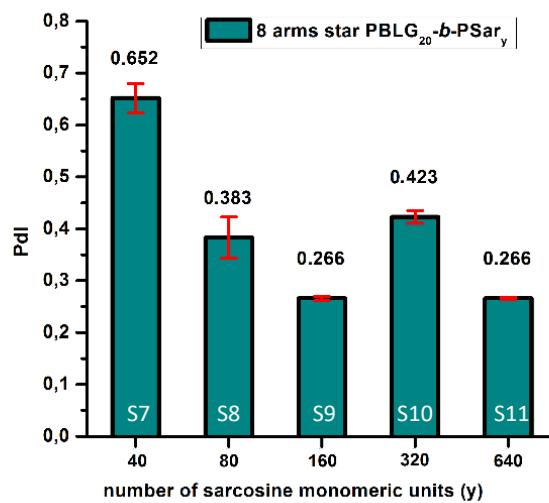


Figure S6. Dispersity index (PdI) of star polypept(o)ides S7-S11 at a concentration of 5 mg/mL in water (error bar represents the standard deviation of three measurements).

Table S1. Hydrodynamic radius (R_H) and dispersity index (PdI) of star polymer nanoaggregates in deionized water (error values represent the standard deviation of three measurements).

Sample	10 mg/1 ml	
	RH (nm)	PdI
8 arm star PBLG ₂₀ -b-PSAR ₂₀	230.7 ± 11.2	0.89 ± 0.04
8 arm star PBLG ₂₀ -b-PSAR ₄₀	434.4 ± 12.1	0.61 ± 0.04
8 arm star PBLG ₂₀ -b-PSAR ₈₀	311.1 ± 4.7	0.4 ± 0.02
8 arm star PBLG ₂₀ -b-PSAR ₁₆₀	179.2 ± 0.9	0.32 ± 0.04
8 arm star PBLG ₂₀ -b-PSAR ₃₂₀	131.9 ± 1.9	0.44 ± 0.01
8 arm star PBLG ₂₀ -b-PSAR ₆₄₀	124.9 ± 4.2	0.27 ± 0.002

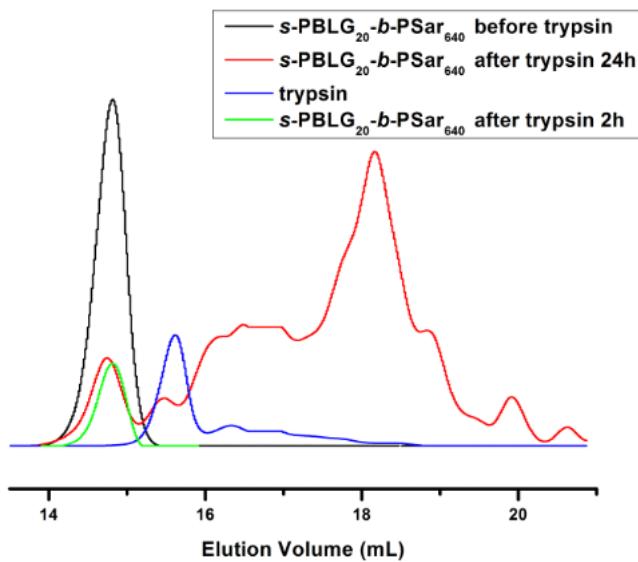


Figure S7. SEC traces of S11 before and after incubation with trypsin.

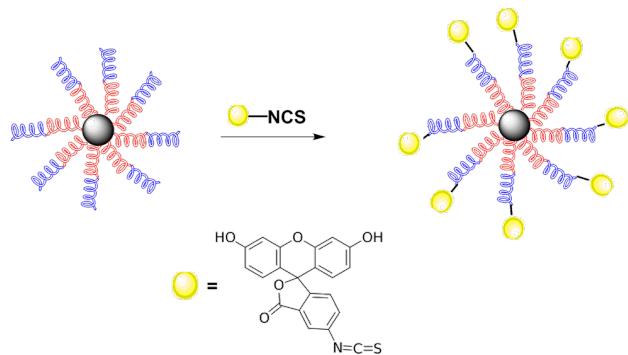


Figure S8. Labelling of S11 with fluorescein isothiocyanate, FITC.



Time (hours)	Absorbance (A)
24	0.145
48	0.003
72	0.005
96	0.001

Figure S9. Left: Images of dialysis to remove excess FITC from S11 after 24 and 96 hours. Right: UV-Vis ($\lambda=495$ nm) absorbance of dialysate demonstrating removal of excess FITC.

Table S2. Experimental data for the mass transport of FITC-S11 through artificial mucus (FITC-S11 + Mucus) and controls without mucus (FITC-S11 – Mucus).

	Cumulative transport (μg)				Percentage of theoretical
	60 min	120 min	180 min	240 min	
Experiment 1					
FITC-S11 + Mucus 1	0.38	1.88	3.20	3.53	35.25
FITC-S11 + Mucus 2	0.26	1.32	2.05	2.39	23.85
FITC-S11 - Mucus 1	2.76	6.27	7.59	8.31	83.12
FITC-S11 - Mucus 2	2.74	6.45	7.60	8.18	81.84
Experiment 2					
FITC-S11 + Mucus 1	1.32	2.27	3.05	4.04	40.37
FITC-S11 + Mucus 2	2.23	3.41	4.25	5.38	53.81
FITC-S11 - Mucus 1	2.16	10.45	9.35	10.19	101.87
FITC-S11 - Mucus 2	3.08	5.65	6.82	8.18	81.78
Experiment 3					
FITC-S11 + Mucus 1	4.30	5.49	6.77	7.55	75.52
FITC-S11 + Mucus 2	1.39	3.52	5.01	8.33	83.28
FITC-S11 - Mucus 1	6.24	8.25	9.41	9.78	97.84
FITC-S11 - Mucus 2	5.90	8.47	9.47	9.97	99.68

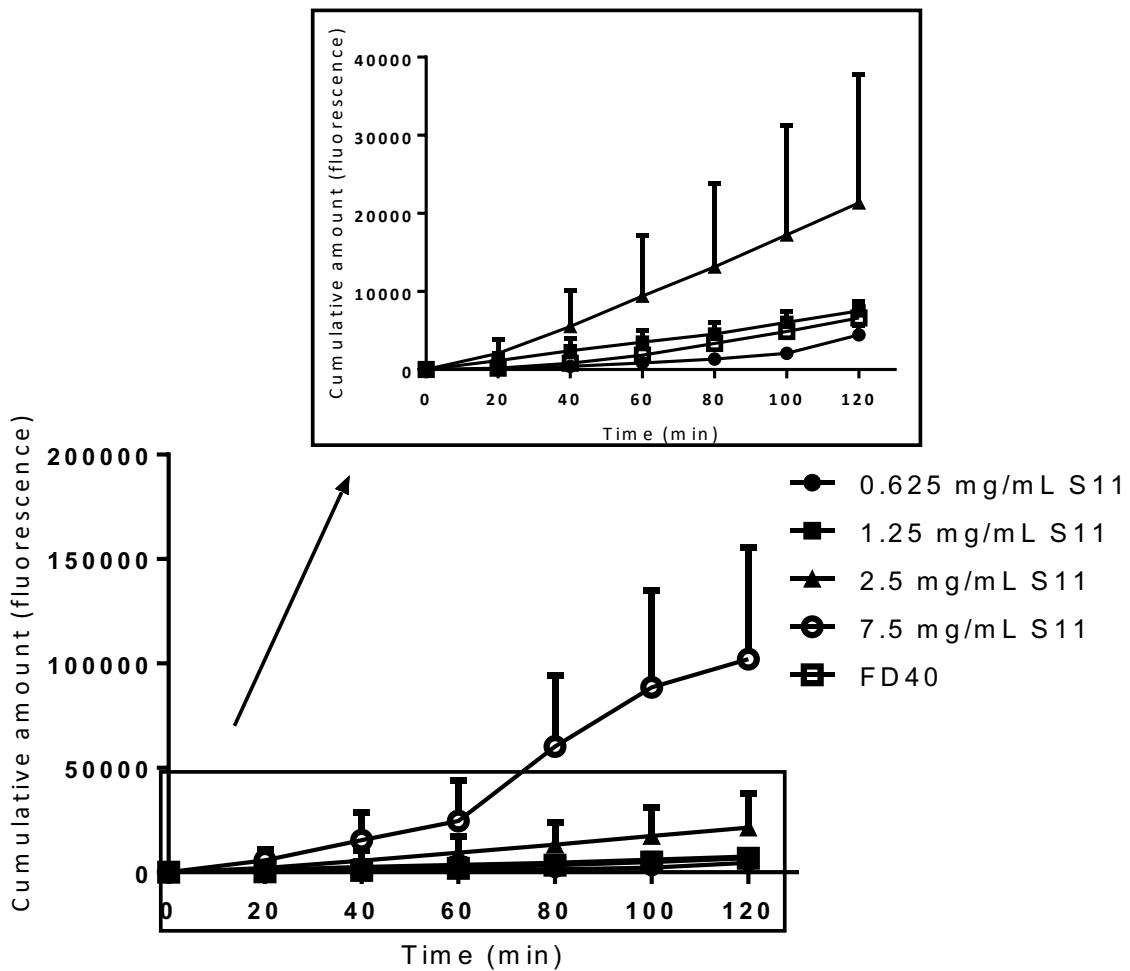


Figure S10. Cumulative permeated signal for 0.625-7.5 mg/mL FITC-S11 (S11) and FD40 (2.5 mg/mL) across rat jejunal mucosae mounted in Franz Cells ($n=3-4$). Inset shows magnification of groups in the absence of the 7.5 mg / mL S11 group.