

# **Breaking the Barrier – Potent Anti-Inflammatory Activity following Efficient Topical Delivery of Etanercept using Thermoresponsive Nanogels**

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## **Supporting Information**

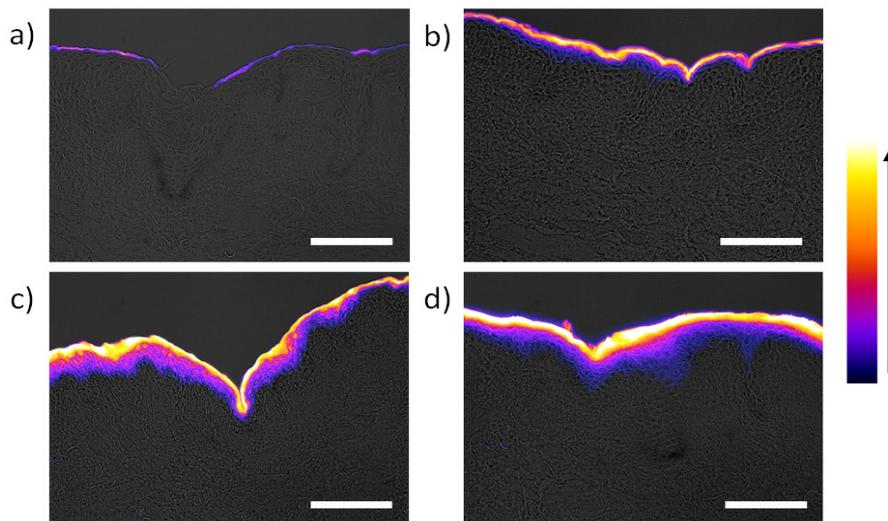
**Table S1.** The synthesised nanogels and their properties.

Nanogel	Size [nm] (PDI) <sup>a</sup>	$\zeta$ potential [mV] <sup>b</sup>	T <sub>cp</sub> [°C] <sup>c</sup>	Loading capacity [wt.%]
tNG_pNIPAM	88.36 (0.231)	-2.540	34.6	-
tNG_pNIPAM_ETR	83.99 (0.243)	-3.040	34.7	10
tNG_tPG	182.7 (0.125)	1.900	32.0	-
tNG_tPG_ETR	185.3 (0.150)	0.341	32.7	10

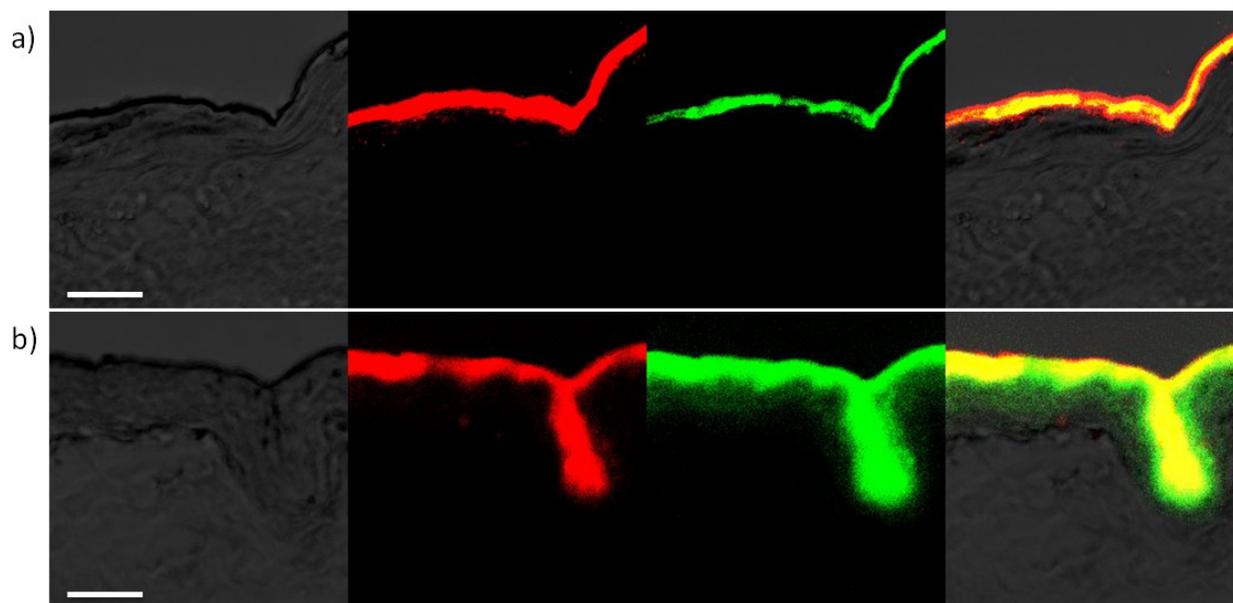
<sup>a</sup> Size and polydispersity index (PDI) by DLS in PBS at 25 °C. Measurements were performed in triplicates; intensity average mean value presented.

<sup>b</sup>  $\zeta$  potential determined by Zeta-sizer in PBS. Measurements were performed in triplicates; intensity average mean value presented.

<sup>c</sup> Cloud point temperature determined as the temperature at 50% transmittance by UV-Vis ( $\lambda = 500$  nm).



**Supplemental Figure S1.** Representative fluorescence imaging of FITC-BSA in human skin biopsies (tape stripped 50x) following 6 h topical application in PBS (a), tNG\_pNIPAM (b), tNG\_pNIPAM\_ETR (c), tNG\_tPG (d). Temperature was increased from 32 to 37 °C in the first 3 h and held there for the remaining incubation. Images show FITC-BSA staining pseudo temperature coloured (scale and direction of intensity indicated to the right) overlaid on differential interference contrast (DIC) images (scale bar = 100 $\mu$ m).



**Supplemental Figure S2.** IDCC-tNG\_tPG (a, b) loaded with FITC-BSA were topically applied to normal (a) and TNF $\alpha$  (b) treated skin equivalents over 3 hours (3 h topical application with temperature ramp). Images show (from left to right) bright field images (grey), tNG staining (red), BSA staining (green) and the overlay of these three images. Scale bar = 25  $\mu$ m.