Supporting Information

A Photoresponsive Hyaluronan Hydrogel Nanocomposite for Dynamic Immunomodulation

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This Supporting Information includes:

Supplemental Figures (Fig. S1-S8) with the captions.

Supplemental Figure S1

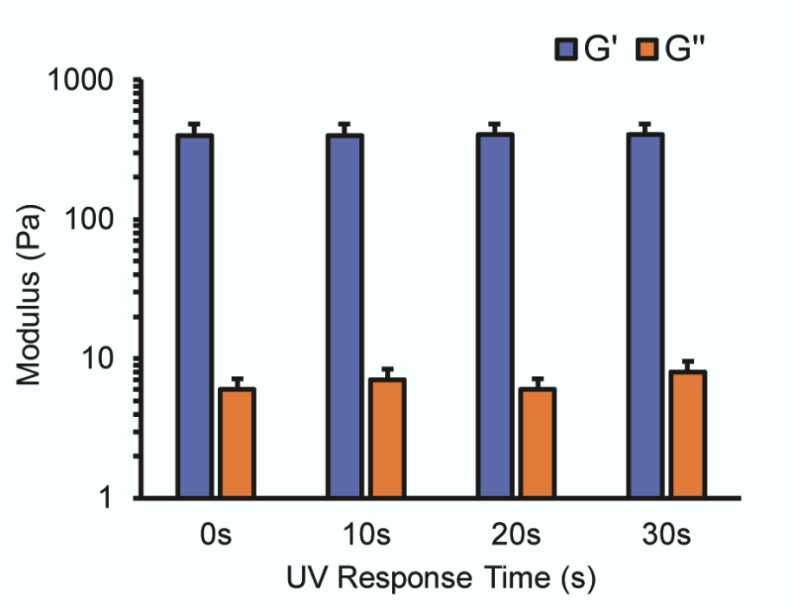

Figure S1. The storage (G') and loss modulus (G") of photo-triggered HA-APP hydrogels. 3-D HA-APP hydrogels underwent photo-controlled RGD peptide release and conjugation for a total 30-second UV exposure time. The moduli were measured with a plate-to-plate rheometer at a constant strain of 0.05 with frequency ranging from 0.1 to 10 rad/s. The data are shown as the mean ±SEM, with the mean represented as averages of G' and G" over the frequency range.

Supplemental Figure S2

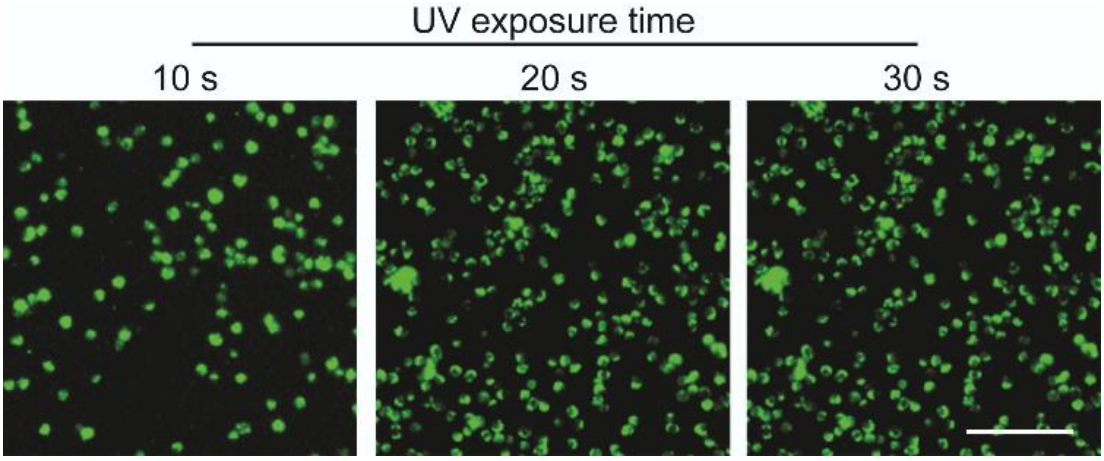

Figure S2. Viability of RAW 264.7 M0 macrophages encapsulated in 3-D HA-APP hydrogels. Live/Dead viability images after 10s, 20s, and 30s of one-time UV exposure during which viability remains consistently high (> 95%). Scale bar is 200 μm.

Supplemental Figure S3

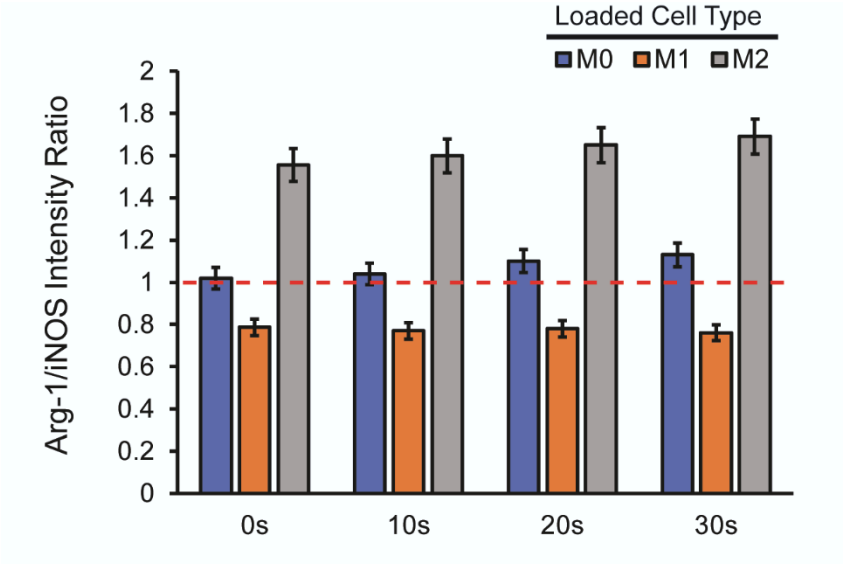

Figure S3. UV exposure alone does not alter macrophage phenotype. Quantified intensity ratio of Arg-1/iNOS in inactivated M0 macrophages and pre-polarized M1 and M2 RAW264.7 macrophages after 72hr encapsulation in 3-D HA hydrogels for different UV exposure times. The data are shown as the mean ±SEM. Error bars represent ± S.E.M. from 3 independent experiments.

Supplemental Figure S4

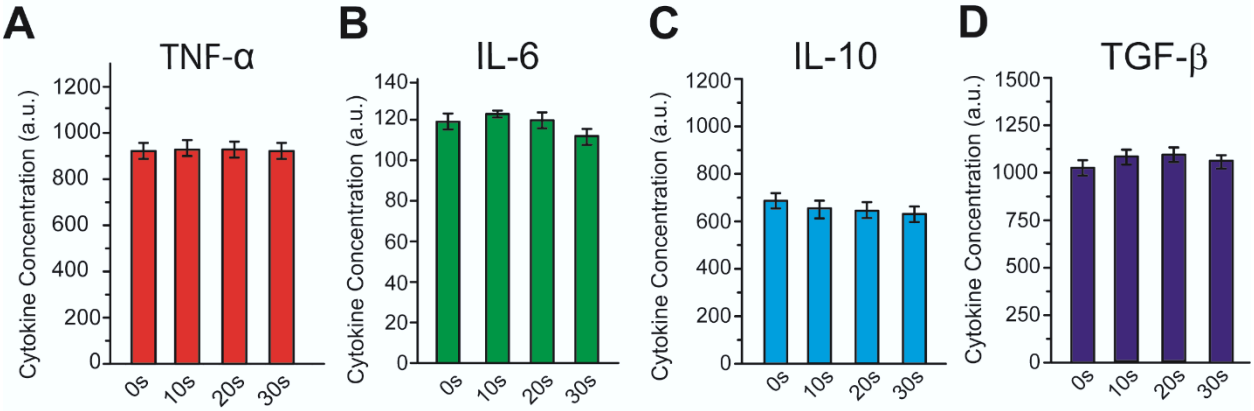

Figure S4. UV exposure alone does not alter macrophage phenotype**.** Immunoassay levels of proinflammatory cytokines, TNF-α (A) and IL-6 (B), and anti-inflammatory cytokines IL-10 (C) and TGF-β (D) secreted by M0 macrophages in 3-D HA hydrogels treated with increasing one-time UV exposure after 72hrs. The data are shown as the mean ±SEM. Error bars represent ± S.E.M. from 3 independent experiments.

Supplemental Figure S5

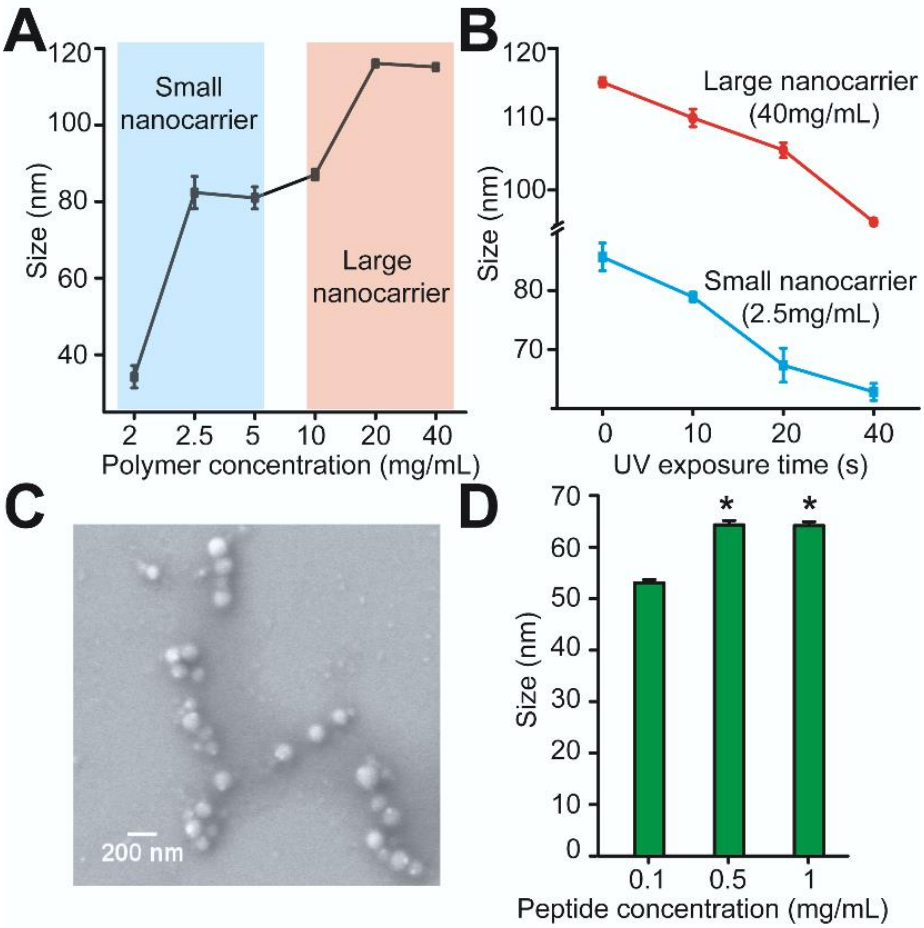

Figure S5. APP nanocomposites characterization. Size characterization of small and large APP nanocomposites based on (A) APP polymer concentration and (B) one-time UV exposure time. (C) representative SEM image of APP nancomposites. Scale bar is 200 nm. (D) Size characterization of APP nancomposites for increasing load of αvβ3 integrin-specific RGD peptides. The data are shown as the mean ±SEM (*, $p < 0.05$). Error bars represent ± S.E.M. from 3 independent experiments.

Supplemental Figure S6

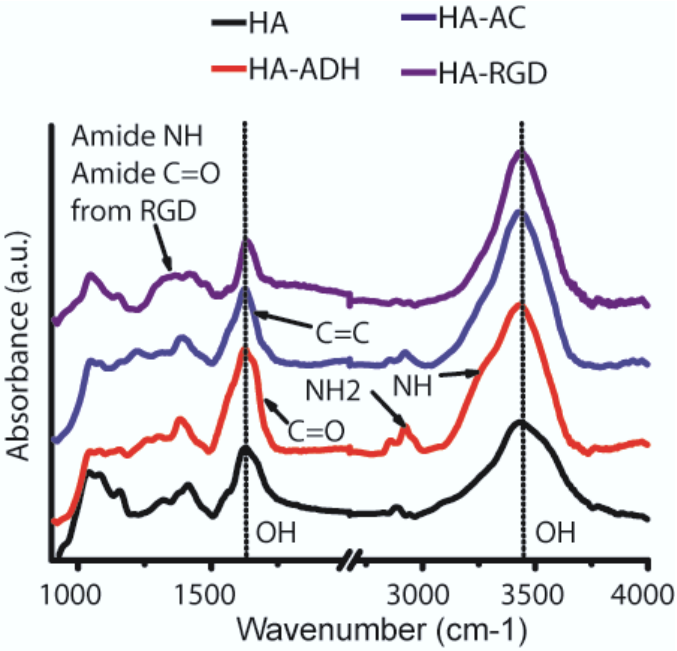

Figure S6. IR spectrum of HA-Ac Macromer synthesis from HA, HA-ADH and HA-Ac intermediate steps, as well as photo-controlled RGD peptide conjugation onto HA-Ac macromer.

Supplemental Figure S7

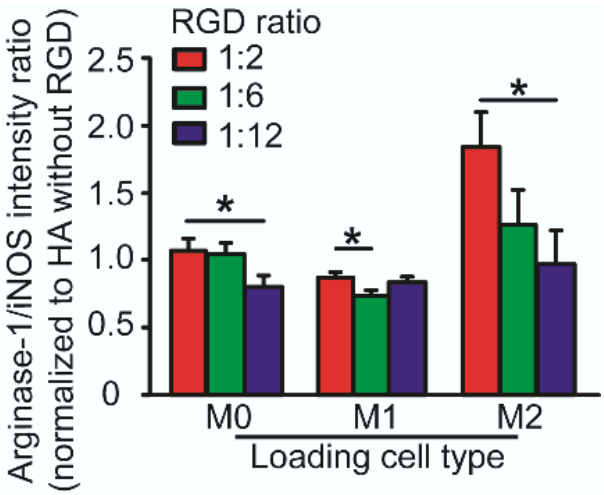

Figure S7. Dose-dependent integrin αvβ3 activation promotes M2 macrophage polarization. Quantified as a fluorescent intensity ratio, Arg-1/iNOS marker expressions of M0, M1 and M2 RAM264.7 macrophages after 72 hr encapsulation in 3-D, static HA hydrogels pre-conjugated with different ratios of RGD peptides. The data are shown as the mean ±SEM (*, $p < 0.05$). Error bars represent ± S.E.M. from 3 independent experiments.

Supplemental Figure S8

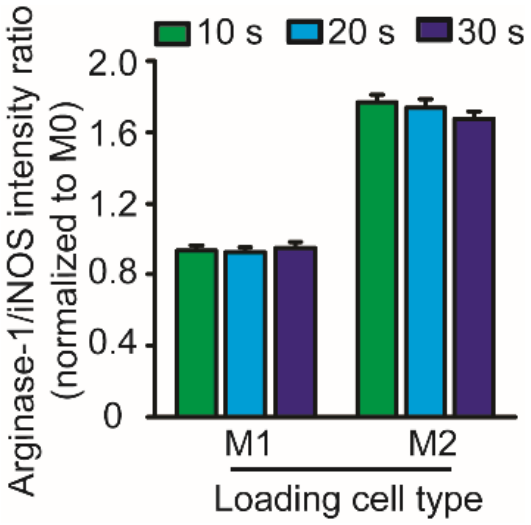

Figure S8. APP nanocomposites without RGD peptide loading cannot alter macrophage phenotype. Quantified intensity ratio of Arg-1/iNOS in polarized M1 and M2 RAW264.7 macrophages after 72hr encapsulation in 3-D HA hydrogels with empty APP nanocomposites and different UV exposure. The data are shown as the mean ±SEM. Error bars represent ± S.E.M. from 3 independent experiments.