Supporting Information

Hydrolytically degradable microgels with tunable mechanical properties modulate the host immune response

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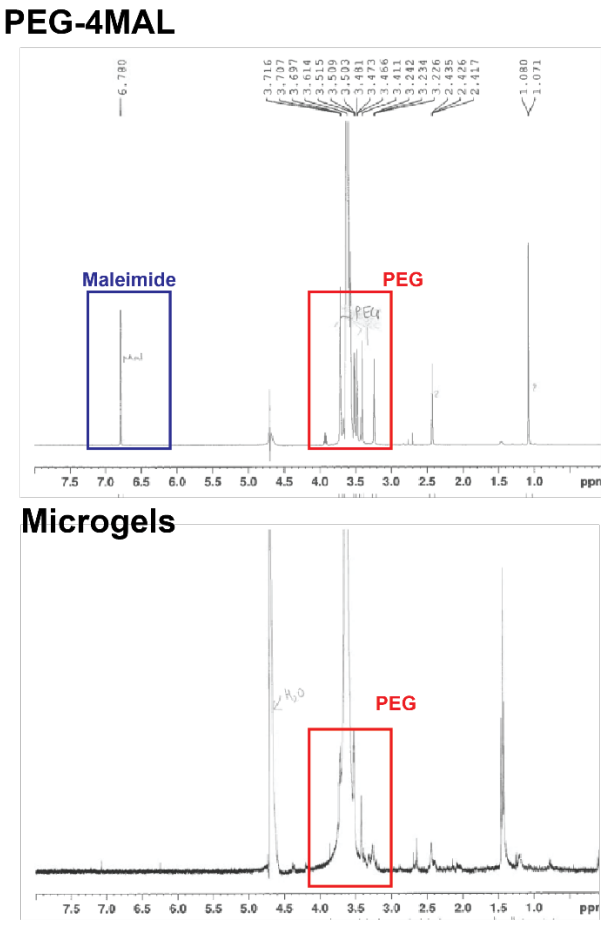

Figure S1. ^{1}H NMR spectra of PEG-4MAL macromer and microgels post-fabrication.

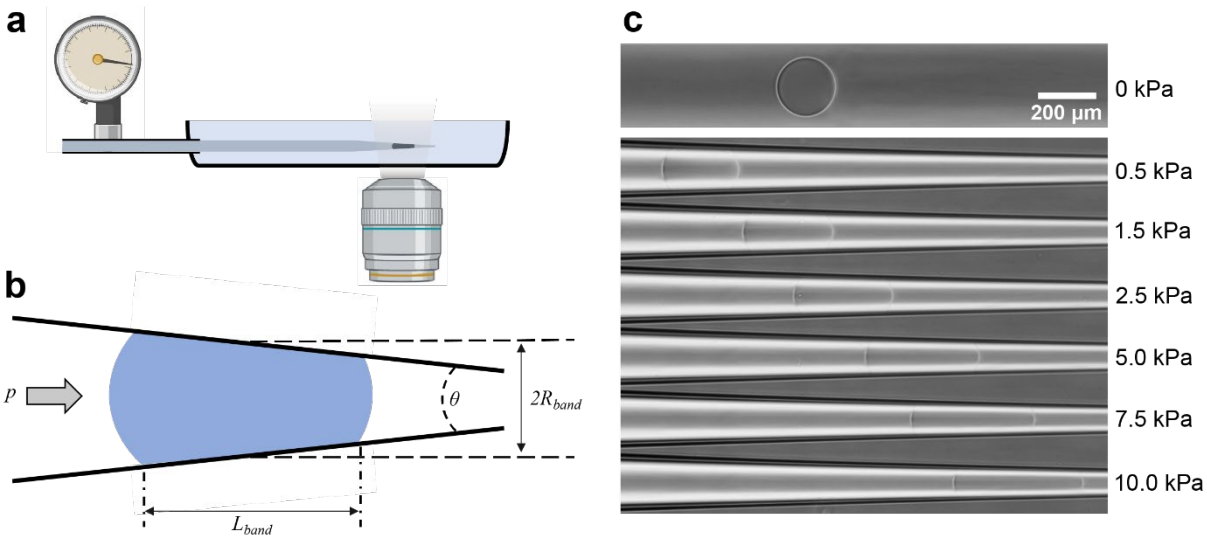

Figure S2. A) Experimental setup for the capillary micromechanics. The tapered glass micropipette (Fivephoton Biochemicals) had the following dimensions: tip inner diameter = 50 µm; base outer diameter = 1.5 mm; length = 5.5 cm; taper style = long. A high precision pressure regulator (Elveflow) applied pressure to the micropipette containing the microgel. The micropipette was immersed in 1% BSA to facilitate optimal flow dynamics. The microgel would deform until it reached equilibrium, when the external applied pressure balanced with the internal elastic stress. A microscope (EVOS) under the micropipette tip acquired images (10X), which were subsequently analyzed in ImageJ. B) Microgel geometry in the tapered region. The microgel was in contact with the walls with an average radius, Rband, and average length, Lband. The taper angle is θ. As the pressure, p, increases, Lband increases and Rband decreases. The elastic properties were calculated from these measurements, as previously described (Wyss et al, Soft Matter, 2010). C) Image series of a microgel deforming in response to increasing pressure.

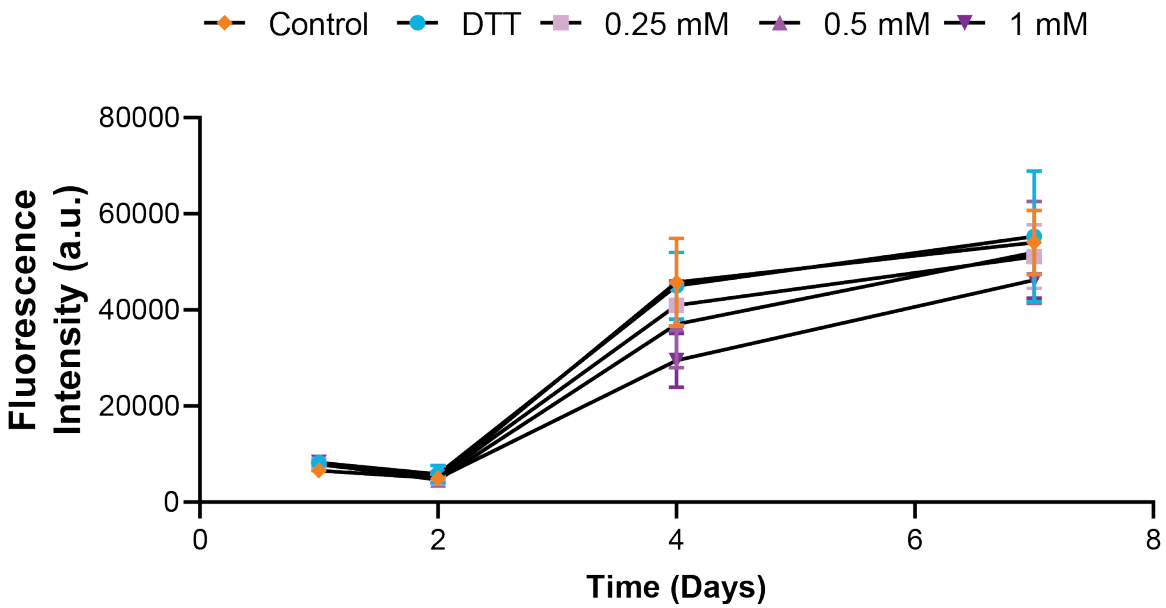

Figure S3. In vitro cytotoxicity of RAW 264.7 macrophage cells treated with all microgel formulations (degradable, and nondegradables). The graph represents cell viabilityduringa 7 day co-culture determined by Alamar Blue assay. Data represents mean standard deviation of the mean (n = 4). No statistical difference found by one-way ANOVA.

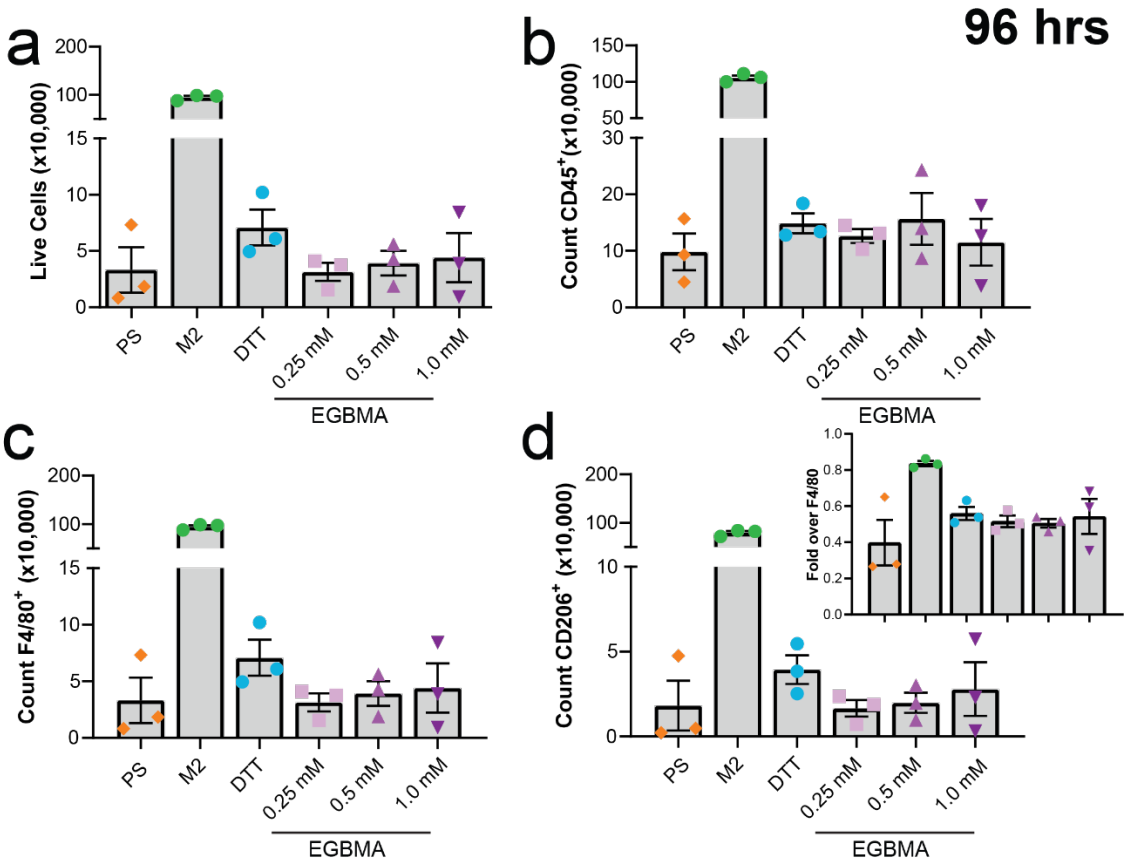

Figure S4. Microgel co-culture with monocytes does not induce activation in the absence of adhesion cues and inflammatory signals. a-d) Cell survival at 96 hr post-incubation does not reveal any changes due to microparticle presence in co-culture.Expression of markers CD45, F4/80, CD206 is consistent across all groups tested. d-inset represents fold expression of CD206 over all cells expression F4/80 in co-culture. All data presented as average ± s.e.m, n=3. Data was analyzed with one-way ANOVA with Tukey corrections for multiple comparisons.

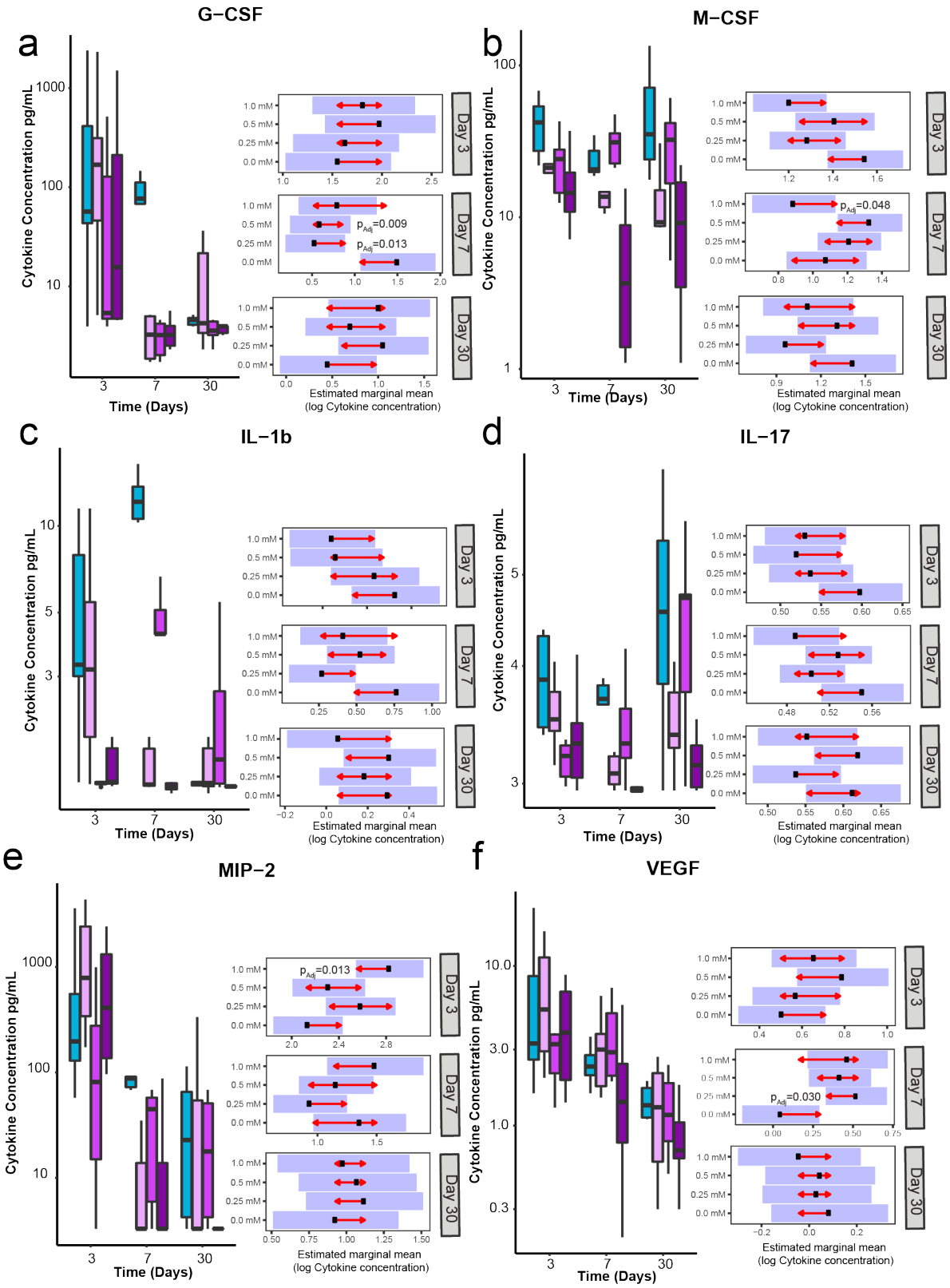

Figure S5. Box plots show cytokine concentrations with raw values plotted on the log10 scale, and estimated marginal means (EMM) comparisons for all time points. n=6 per group.

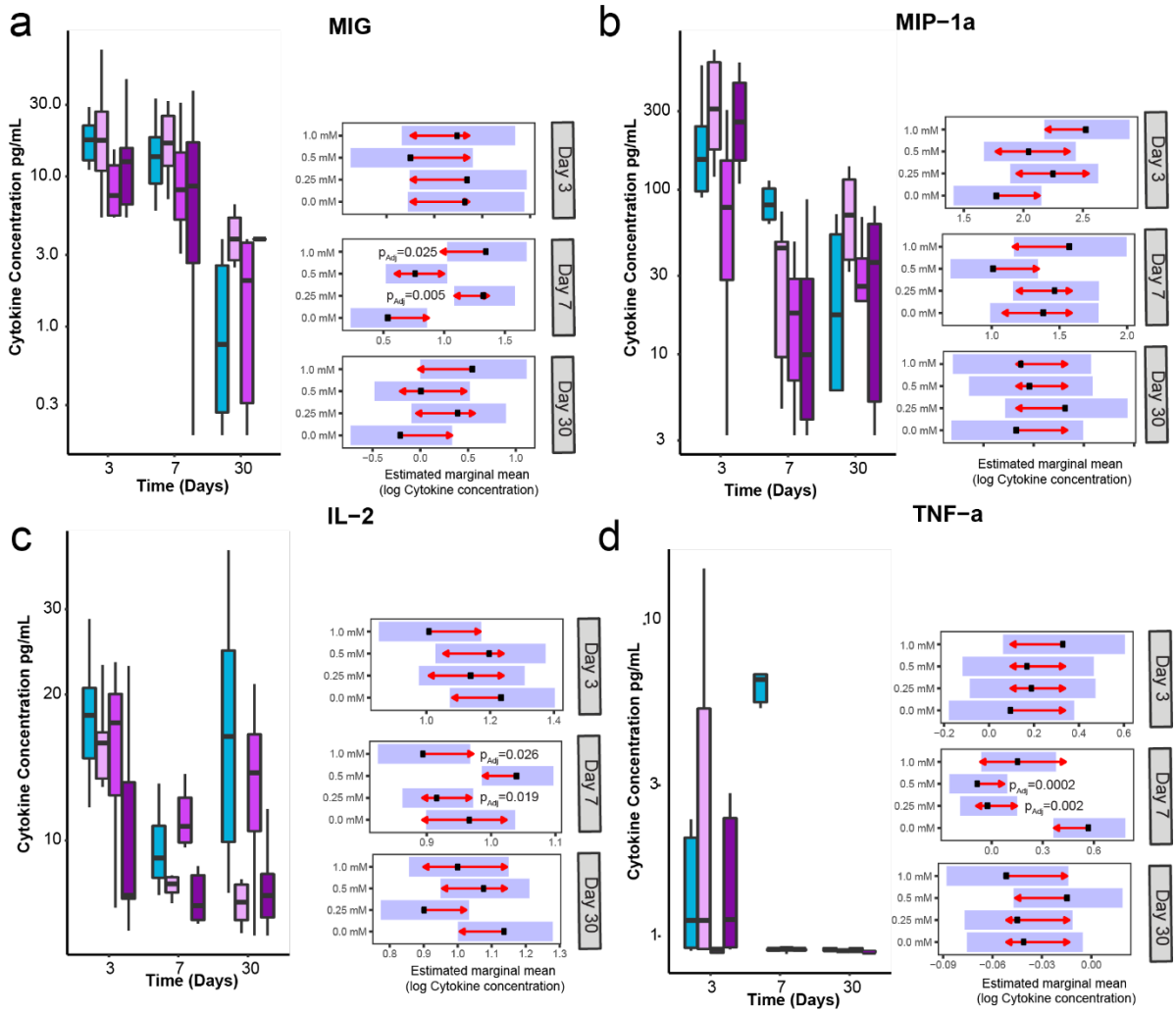

Figure S6. Box plots show cytokine concentrations with raw values plotted on the log10 scale, and estimated marginal means (EMM) comparisons for all time points. n=6 per group.

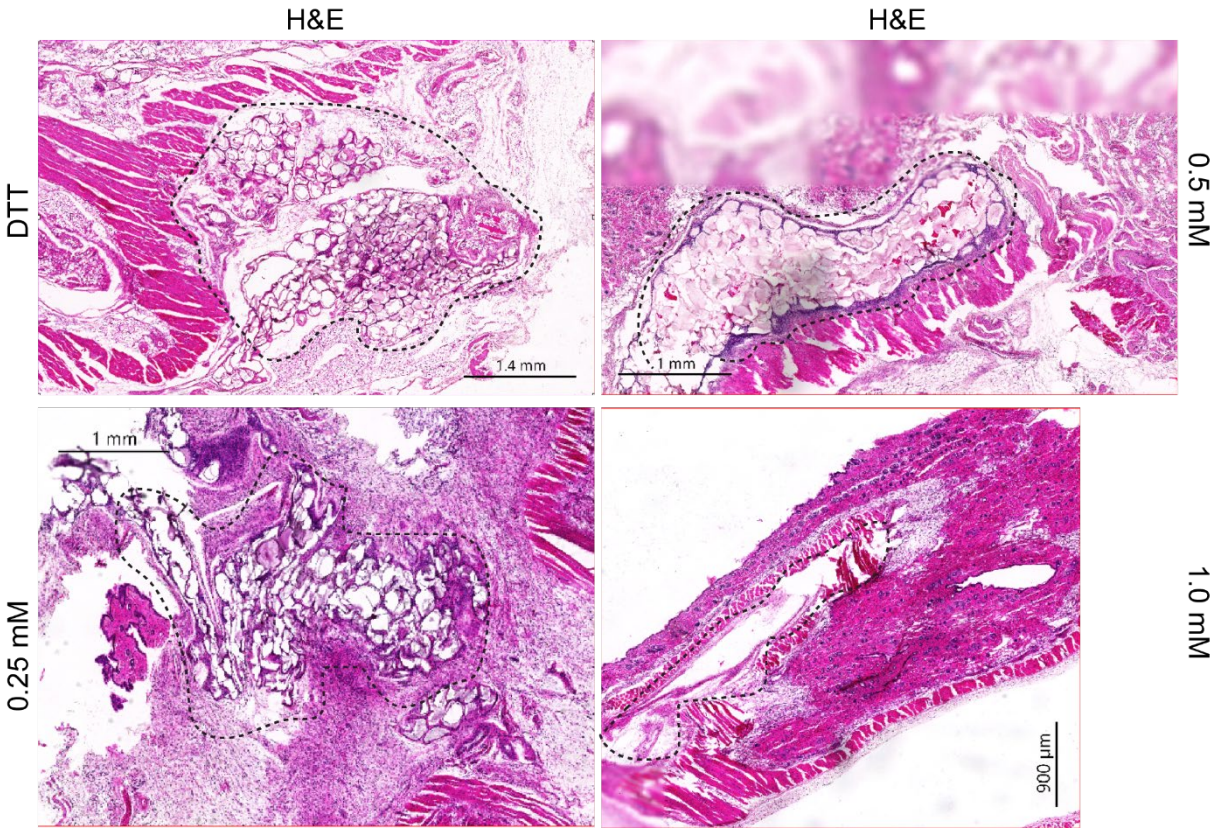

Figure S7. H&E staining at day 30 post-implant of microgels injected in the dorsal subcutaneus space.

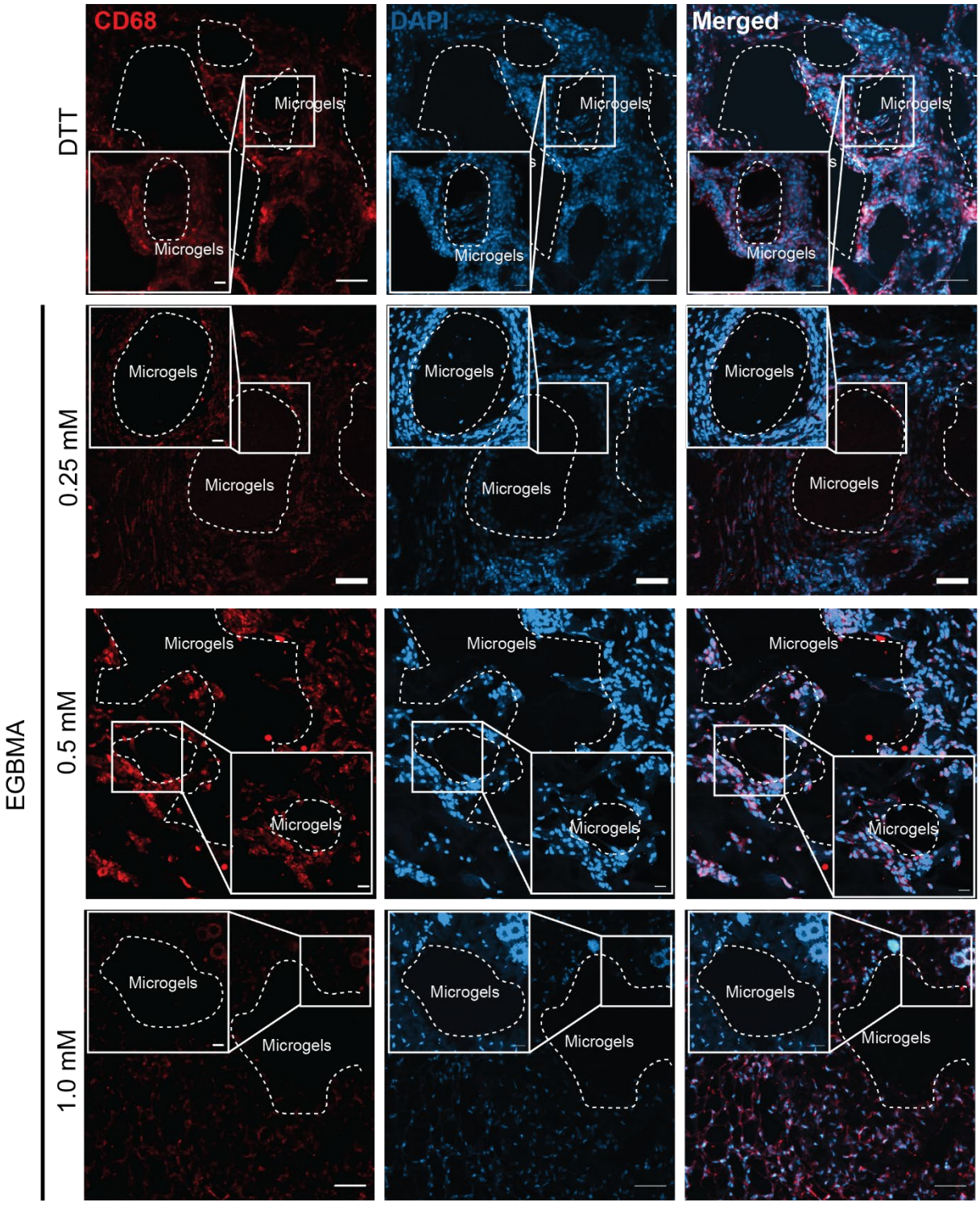

Figure S8. Immunohistochemistry assessment of dorsal microgel implants after 30 days post-injection. Samples were stained for pan macrophage marker CD68 (red) and a nuclear marker DAPI (blue). Microgel area represented by white dashed lines. Inset represents a 20X representative image of area surrounding the microgel. Scale bar of inset 20 µm, 10X image 50 µm.