

Supplementary Figures

Dissolvable Microneedle Patch enables Local Delivery of Immunomodulatory Microparticles Containing Bifunctional Molecules for Periodontal Tissue Regeneration

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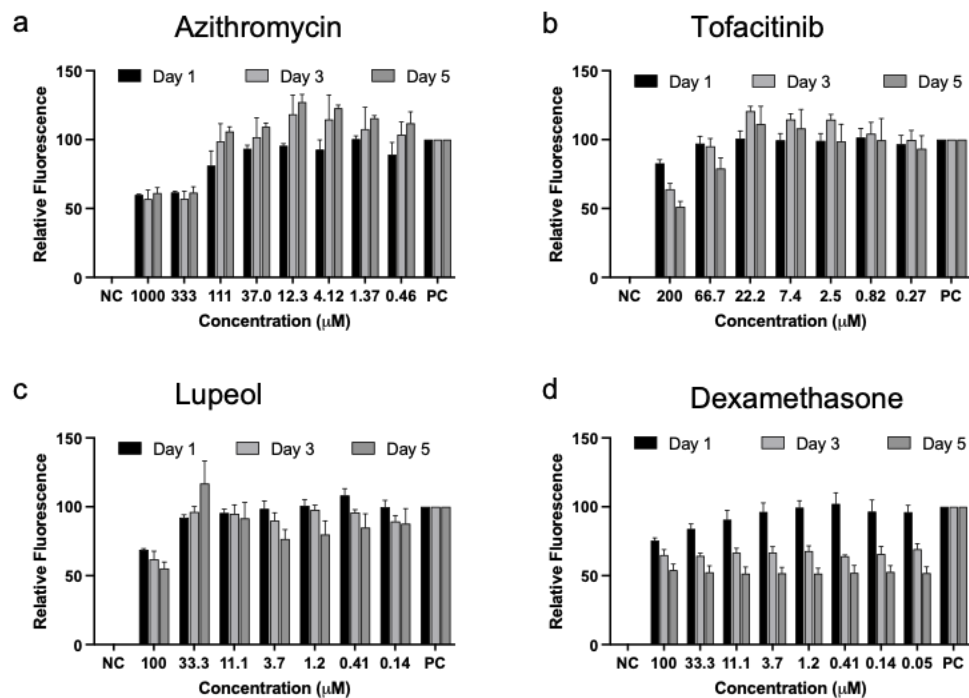
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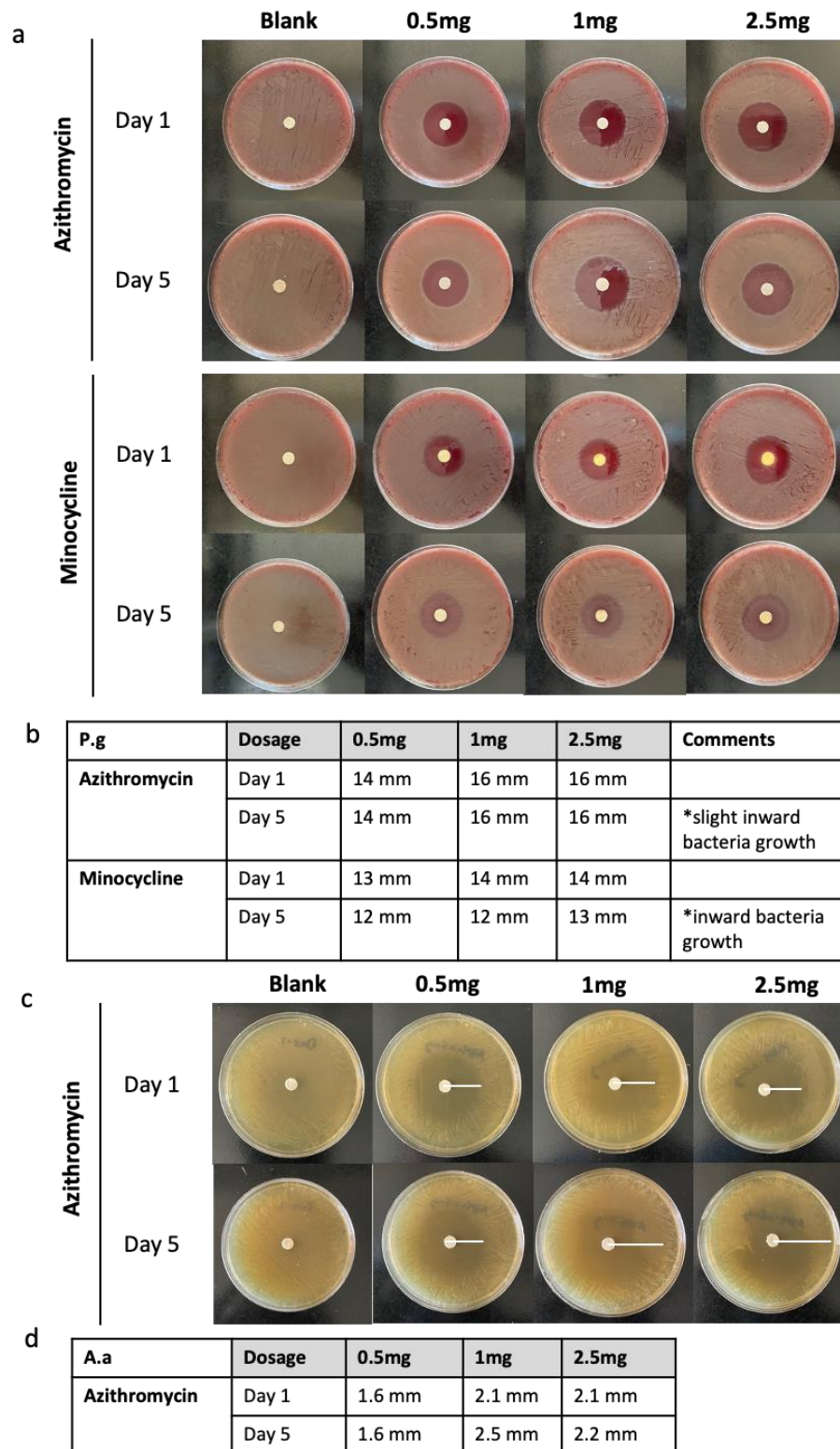
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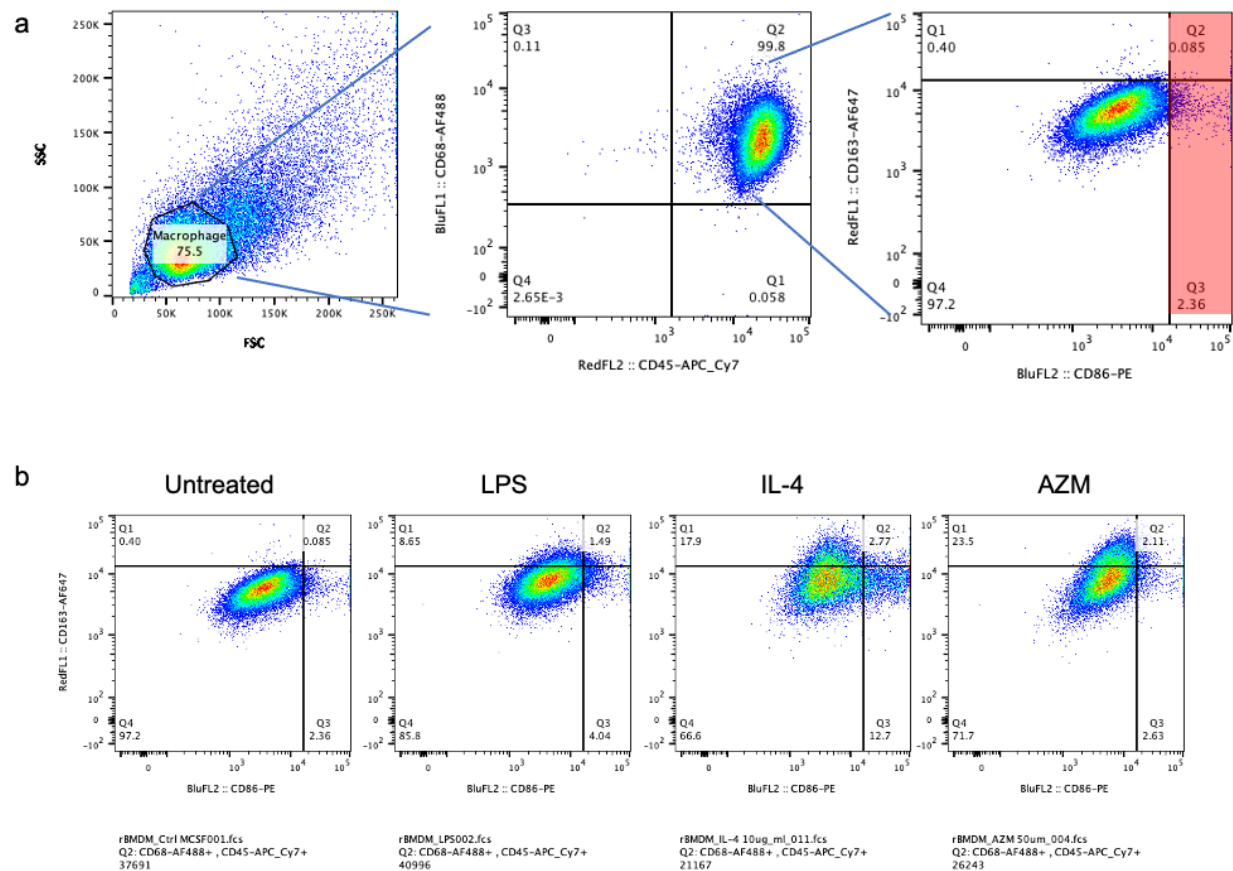
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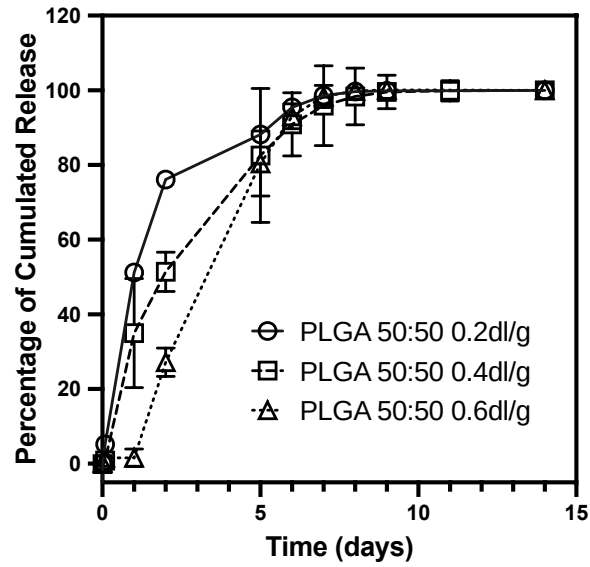
Supplementary Figure 1. Cytotoxicity of immunomodulators. **a**, azithromycin, **b**, tofacitinib, **c**, lupeol and **d**, dexamethasone. PrestoBlue cell viability reagent was used to measure cytotoxicity at day 1, 3, and 5 post compound treatments. Fluorescence was determined using a plate reader at an excitation wavelength of 560 nm and emission wavelength of 590 nm. All data are presented as mean $\pm$ SD (n = 3).



Supplementary Figure 2. Antibacterial effects of azithromycin on *P. gingivalis* and *A.a.* plate culture.
a-b, Image and quantification of inhibition zones on day 1 and day 5 for azithromycin and minocycline on *P. gingivalis* and *A.a.*. **c-d**, Image and quantification of inhibition zones on day 1 and day 5 for azithromycin on *A.a.*

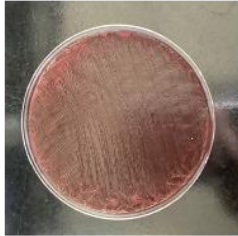


Supplementary Figure 3. Flow cytometry analysis gating strategy. **a**, Gating strategy for CD163⁺CD45⁺CD68⁺ macrophages. **b**, Examples of each group with CD86 and CD163 displayed on the x- and y- axis, respectively.

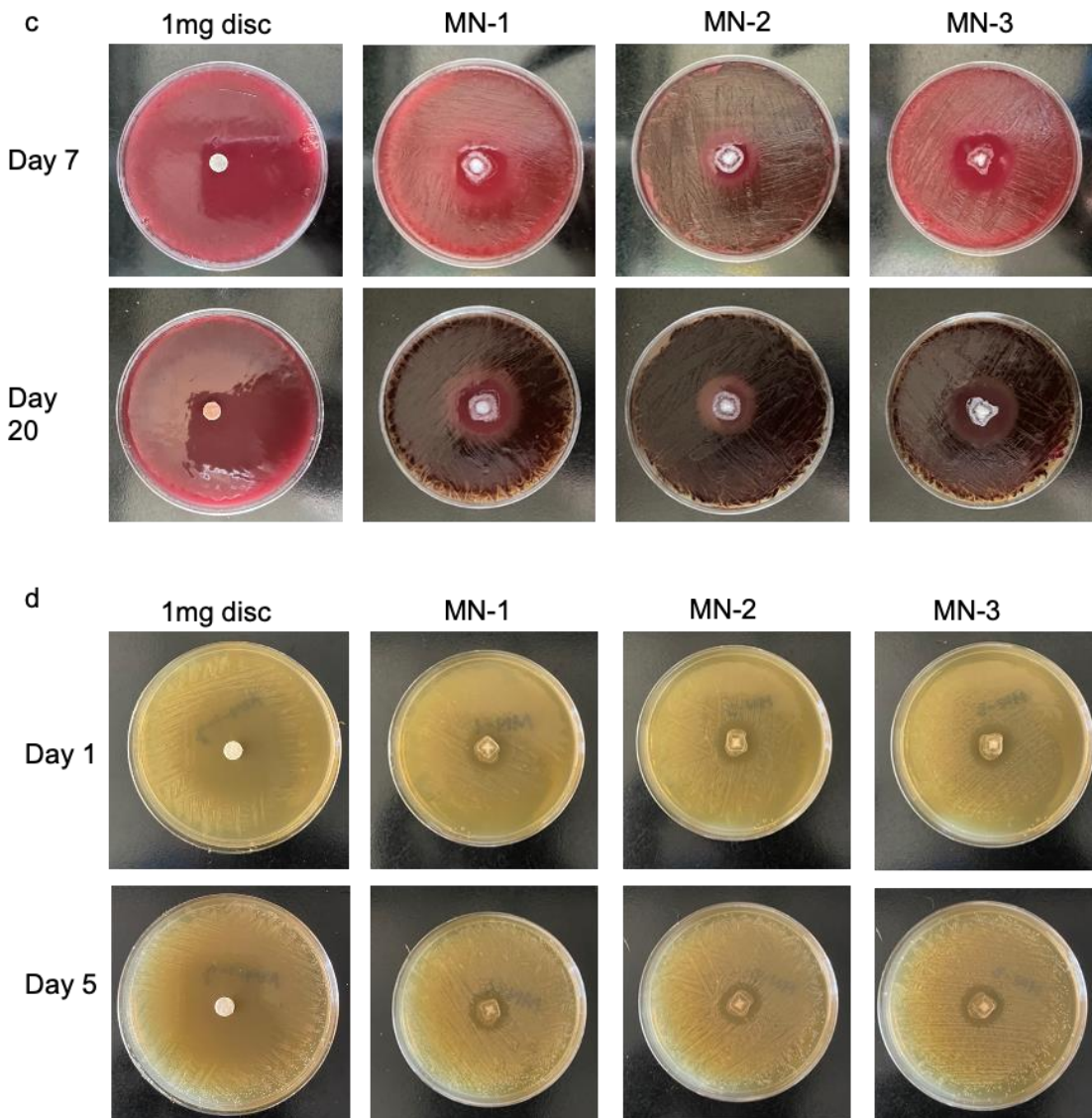


Supplementary Figure 4. Release profile from PLGA of various densities. Rhodamine B was dissolved in PLGA solution and made into microparticles using single emulsion method. Rhodamine B PLGA microparticles (1mg) were incubated in 1ml of PBS at 37°C and supernatants were collected for 14 days. All data are presented as mean $\pm$ SD (n = 5).

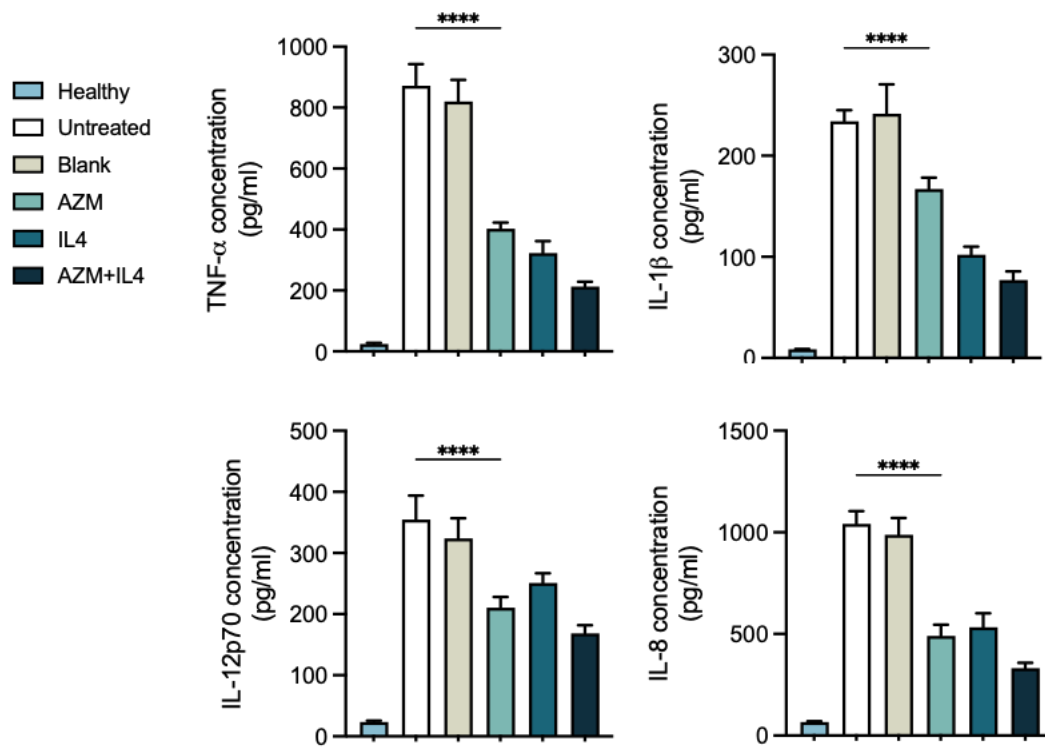
a Control *P.gingivalis*



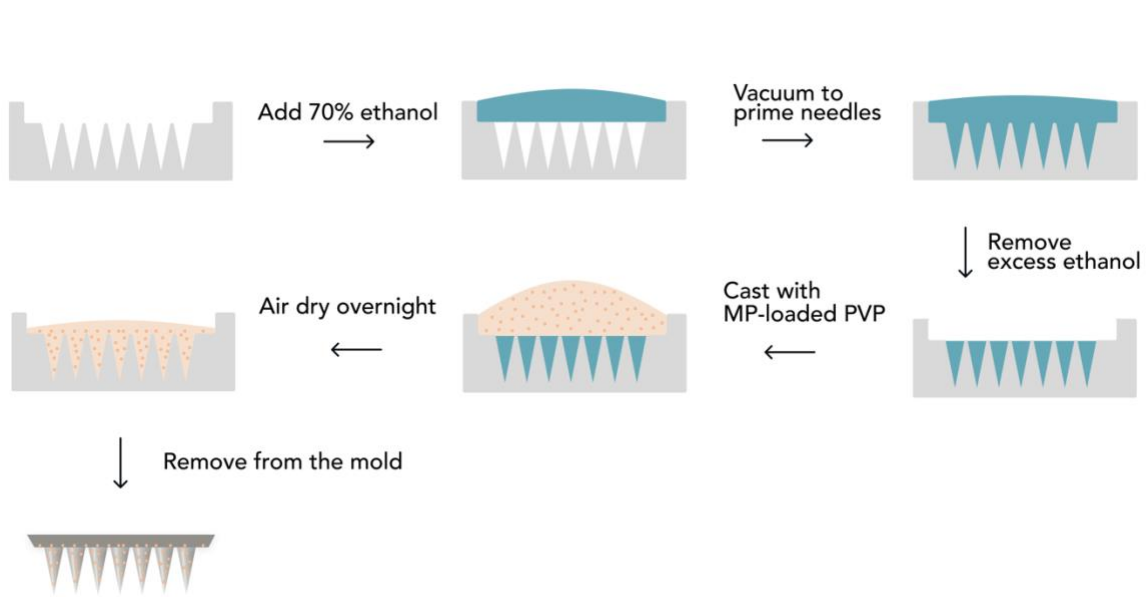
b Control *A. actinomycetemcomitans*



Supplementary Figure 5. Antibacterial effects of azithromycin on *P. gingivalis* and *A.a.* plate culture. **a-b**, Untreated control image of bacteria growth on agar plate for *P. gingivalis* and *A.a.* **c-d**, Inhibition zone of AZM-MN on agar plates with triplicates shown.



Supplementary Figure 6. Immunomodulatory effects of azithromycin microarray patch in vitro. Murine primary monocytes were activated with IFN- γ /LPS and treated with azithromycin (AZM) and IL-4-based microneedles. Cytokine production was measured by bead ELISA at 24 hour post treatment, n= 4-5. Results were analyzed by using t-test. Statistical significance is indicated by asterisks: *p < 0.05, **p < 0.01, and ***p < 0.001.



Supplementary figure 7. Microneedle fabrication strategy. The microneedle patches were fabricated using a vacuum method.