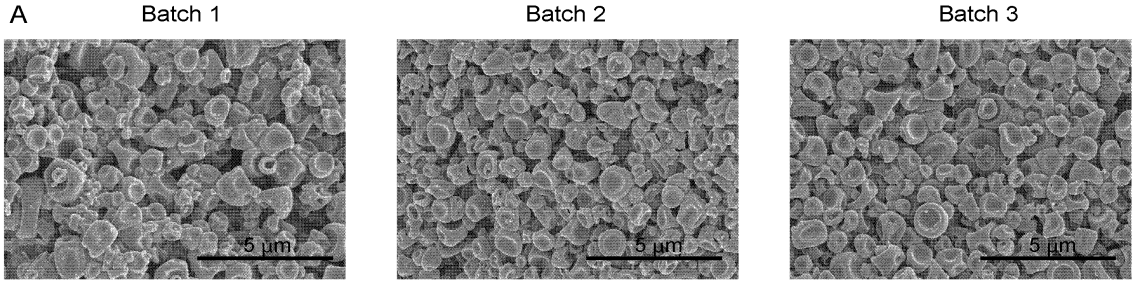
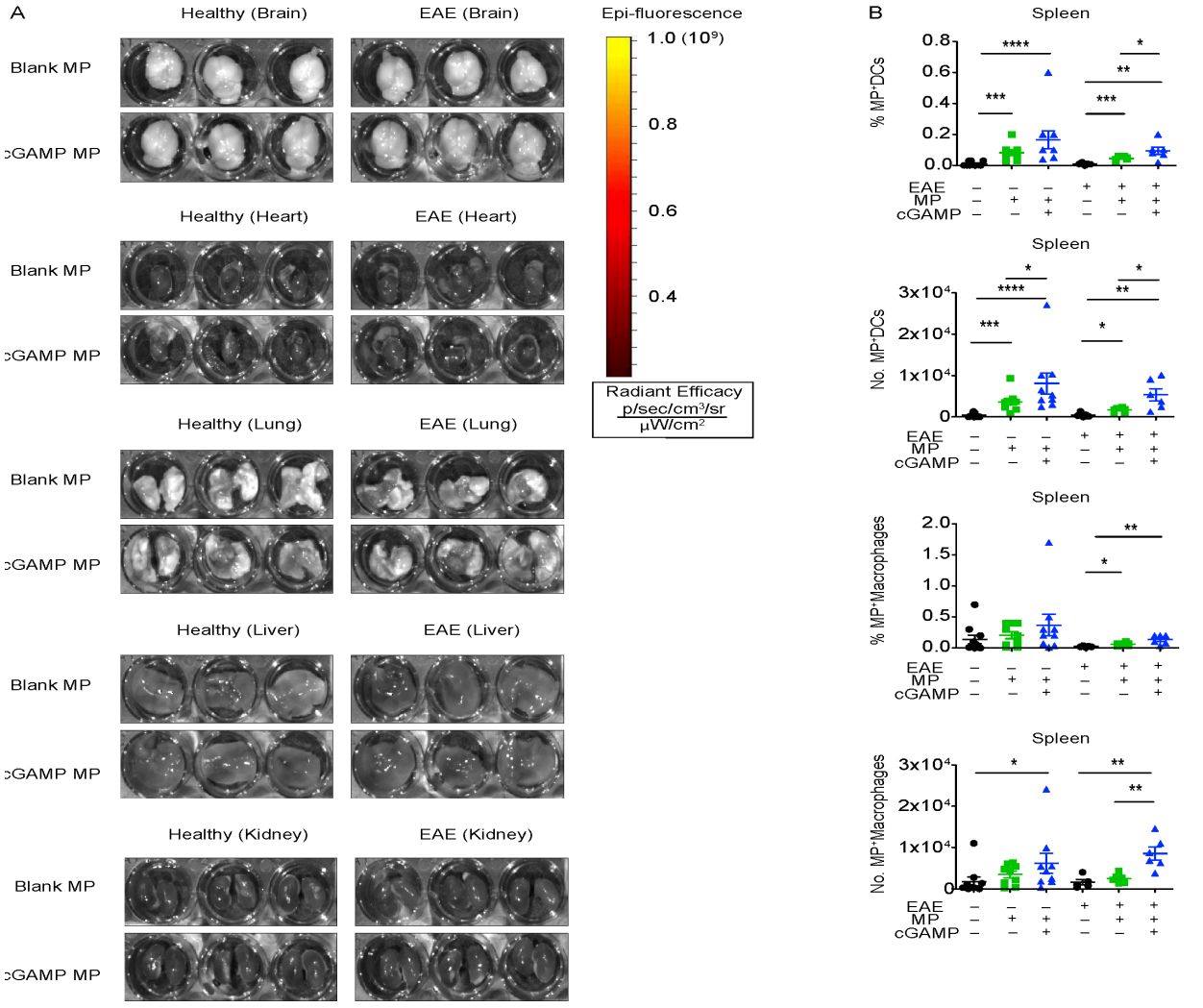
A




B

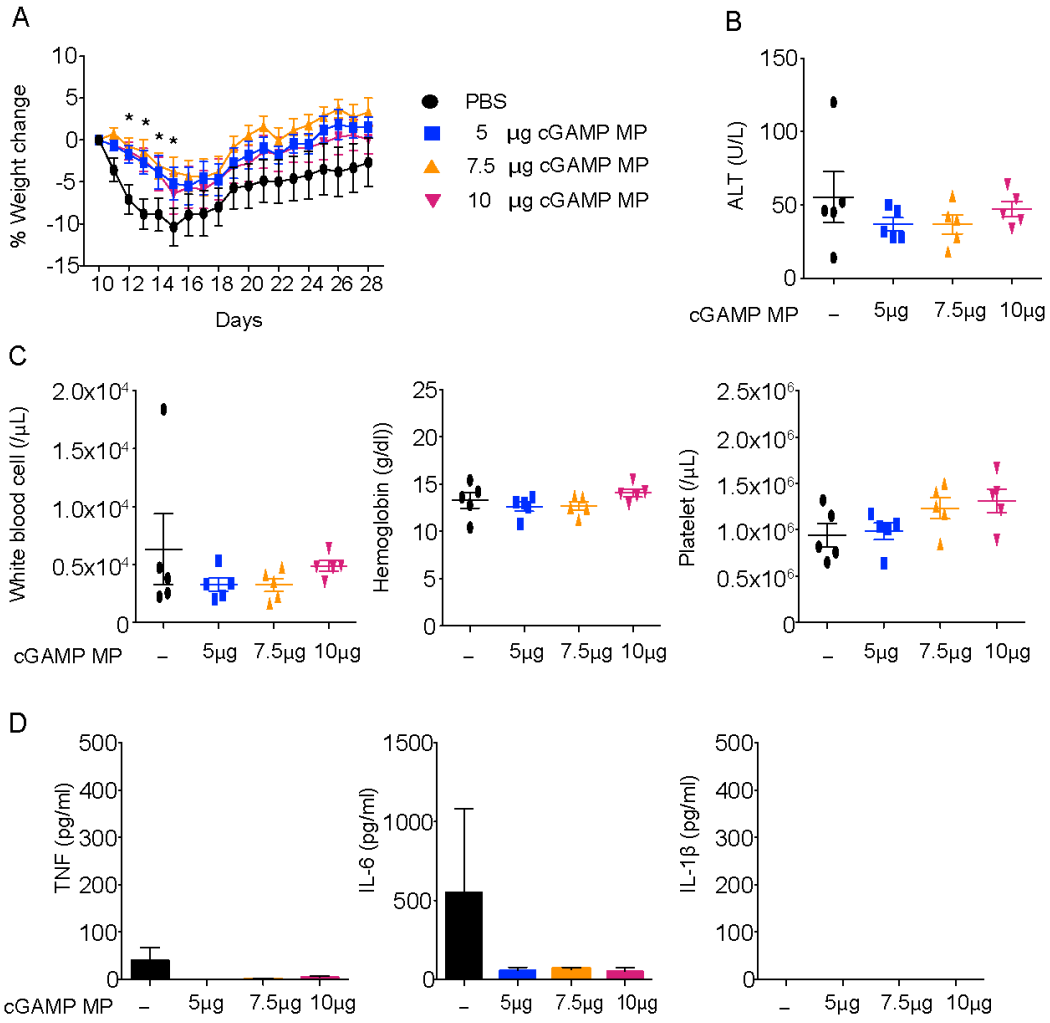
| cGAMP MP Batch # | cGAMP Loading (µg/mg) | Hydrodynamic Diameter by Volume (µm) | Polydispersity Index | Zeta Potential (mV) |
|---|---|---|---|---|
| 1 | 7.3 ± 1.5 | 0.94 ± 0.11 | 0.24 ± 0.08 | –34.5 ± 2.7 |
| 2 | 8.3 ± 0.2 | 0.83 ± 0.05 | 0.22 ± 0.06 | –37.0 ± 5.6 |
| 3 | 8.0 ± 0.1 | 0.96 ± 0.14 | 0.20 ± 0.06 | –32.8 ± 2.5 |

**SUPPLEMENTARY FIGURE 1.** cGAMP MPs were produced with limited physical variability between batches. Three batches of cGAMP MPs were formulated by encapsulating cGAMP in polymerized acetalated dextran using an electrospray method. (A) Formulated cGAMP MPs were sputter coated with AuPd and imaged by scanning electron microscopy. (B) Tabular data of different batches of cGAMP MPs. cGAMP loading was measured by HPLC. Particle size, poly-dispersity, and surface charge were measured by a ZetaSizer.

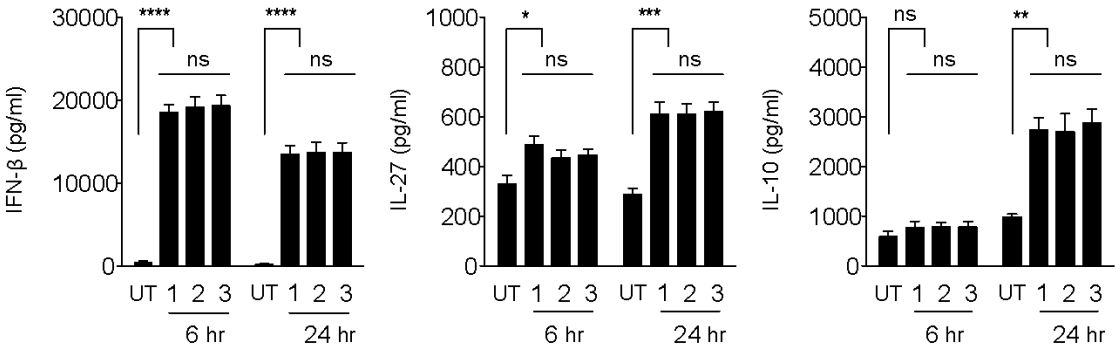



**SUPPLEMENTARY FIGURE 2.** Trafficked particles were detectable only in lymphoid organs

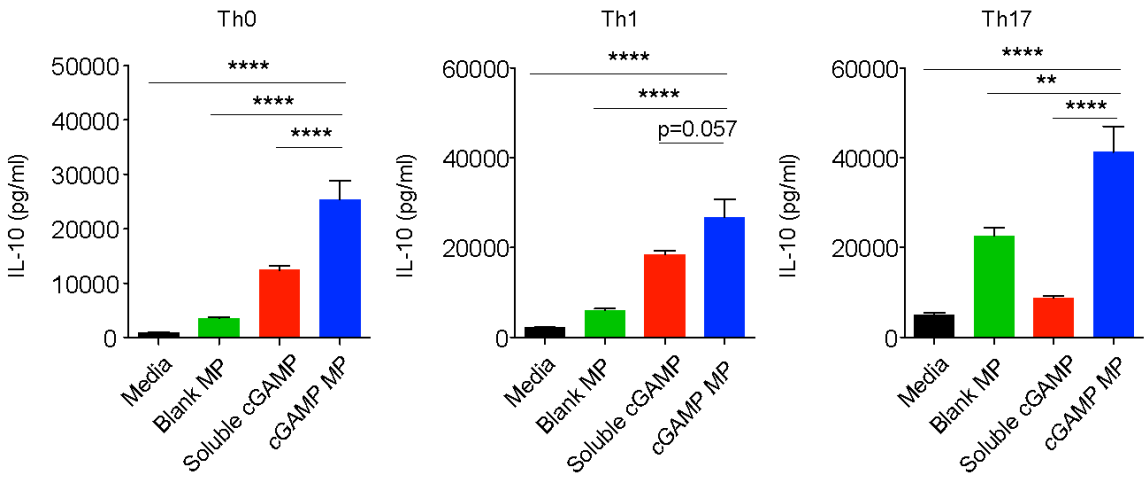
(A, B) Particles (5 µg of cGAMP) or equivalent Blank MP and soluble cGAMP were injected i.m. into the hind leg of healthy or EAE induced mice at days 9,11 and 13 post-disease induction. Mice were euthanized three days post-final injection. (A) Representative fluorescent images of mouse organs as labeled. (B) Flow cytometry analysis of spleen including surface markers of DCs and macrophages with the detection of fluorescent MPs. Combined data of two experiments were tested for significance by Mann-Whitney U tests (n=6-9). *p<0.05 **p<0.01 ***p<0.001 ****p<0.0001. Data is presented as mean ± SEM.




**SUPPLEMENTARY FIGURE 3.** cGAMP MP therapy did not cause toxicity. (A-D) WT mice were treated with increasing doses of cGAMP MPs at Days 9,11,13,15 and 17 post-EAE induction. (A) Mouse weight change beginning at disease onset. (B-D) Whole blood or serum measurements at Day 28 including (B) alanine transaminase concentration (C) white blood cell counts, hemoglobin concentration, platelet counts, and (D) TNF, IL-6, and IL-1β concentrations. Representative data of two independent experiments (n=5-10) evaluated by Mann-Whitney U test *p<0.05 **p<0.01 ***p<0.001 ****p<0.0001. Data is presented as mean ± SEM.




**SUPPLEMENTARY FIGURE 4.** Independently produced cGAMP MPs batches confer biological reproducibility. One hundred thousand BMDCs were stimulated for 3 h with LPS prior to the addition of 0.2 μg/ml cGAMP MPs for 24 hrs. Supernatants were collected at 6 and 24 hrs and evaluated for IFN-β, IL-27, and IL-10. Data combined of two independent experiments (n=5). Batches were evaluated for differences by one-way ANOVA. *p<0.05 **p<0.01 ***p<0.001 ****p<0.0001. Data is presented as mean ± SEM.




**SUPPLEMENTARY FIGURE 5**. cGAMP MP induced IL-10 in CD4 T-cells and in polarized conditions. CD8-depleted splenocytes were added to plates with soluble αCD3 mAb and treated with 5 μg/ml cGAMP MPs for 3 days for Th0 conditions. In other conditions, in addition to αCD3 mAb, cells were polarized to Th1 with 10 ng/ml IL-12p70 or to Th17 with 1 ng/ml TGF-β and 20 ng/ml IL-6. Combined data of at least two experiments (n=6-9). Groups were compared by one-way ANOVA. *p<0.05 **p<0.01 ***p<0.001 ****p<0.0001. Data is presented as mean ± SEM.