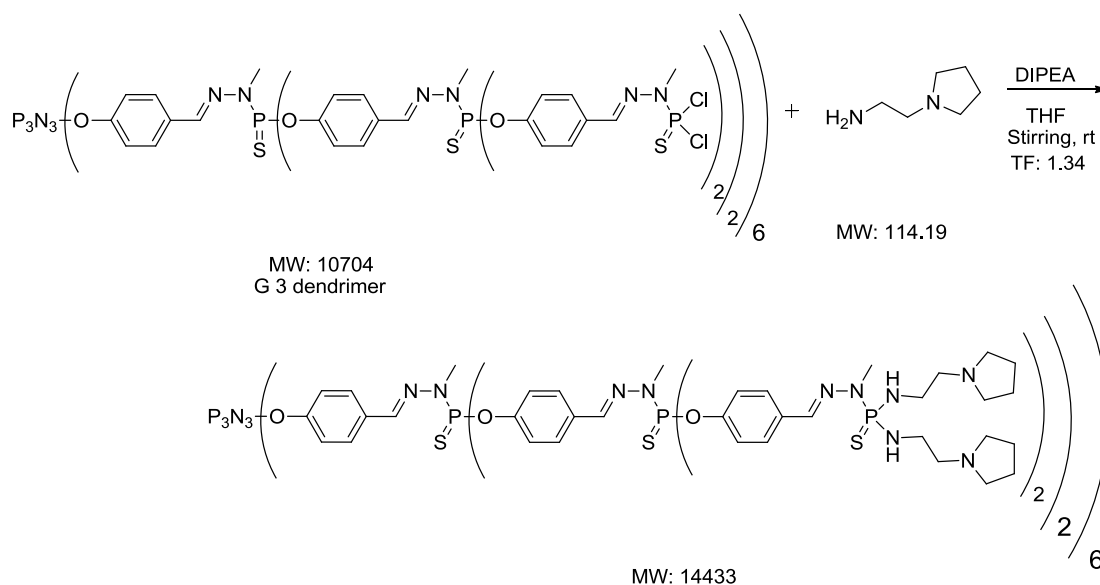


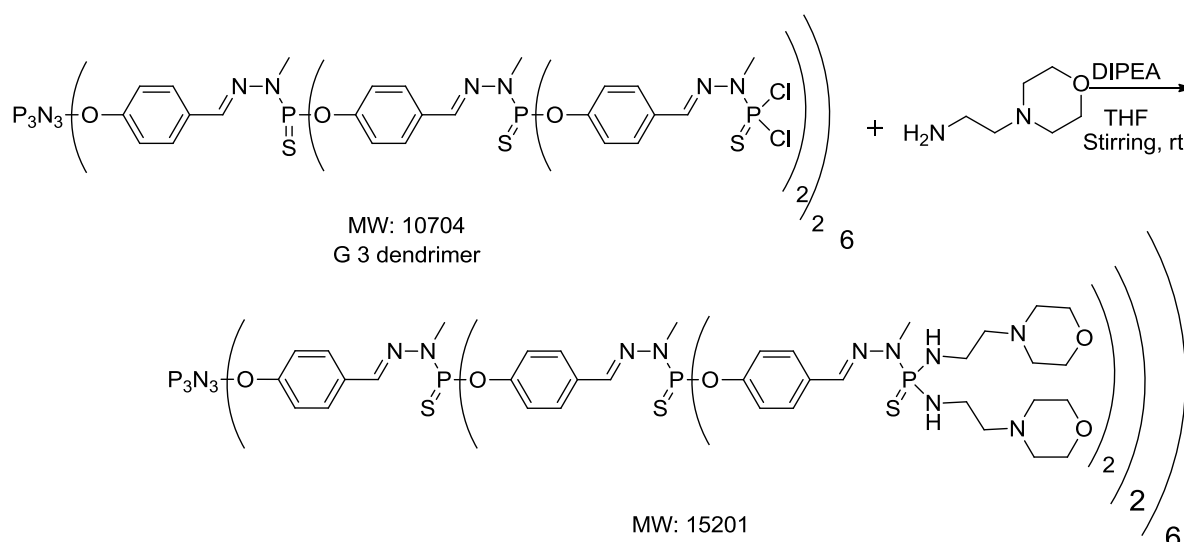
Supplementary material and methods

Dendrimer synthesis



Procedure for DP dendrimer: G 3 dendrimer (0.5g, 0.0467 mmol) and anhydrous magnesium sulphate (0.5g, 4.15 mmol) were dissolved in 20 ml THF. The solution was cooled to 0°C. To this solution DIPEA (0.603ml, 3.362mmol) and aminoethyl pyrrolidine (266.20 mg, 2.335 mmol) were added and stirred for 4 to 6 hours. Control was performed by ³¹P NMR for peak at 68 ppm. After completion of the reaction solvent was evaporated under vacuum and solid residue was extracted with DCM (100 ml) and 20% potassium carbonate solution in water (100ml). The organic layer was dried over sodium sulphate evaporated under reduced pressure. Residue was again dissolved in 10 ml of THF and precipitated in 100 ml pentane, and subsequently stirred for 2h and then filtered under argon. The resulting white powder was dried under vacuum to obtain the desired product as white powder (0.4g, 0.027mmol) in 59.3% yield.

³¹P NMR (161 MHz, CDCl₃) δ = 68.38 (s), 62.74 (s), 62.51 (s), 8.16 (s). ¹H NMR (300 MHz, CDCl₃) δ = 7.72-7.62 (m, 54 H), 7.55 (d, J = 9.0 Hz, 48 H), 7.44(s, 24H), 7.23-7.16 (m, 72 H), 7.01-6.98 (m, 12 H), 4.07-4.02 (m, 48H), 3.31-2.99 (m, 222H), 2.63-2.47 (m, 288H), 1.69 (s, 192H). ¹³C NMR: 151.31 (d), 150.53 (d), 135.32 (d), 133.25 (s), 128.31 (s), 127.50 (s), 121.77 (s), 121.56 (d), 56.18 (d), 53.77 (s), 39.78 (s), 33.13 (d), 30.70 (d), 23.54 (s).



Procedure for DM dendrimer: G 3 dendrimer (0.5g, 0.0467 mmol) and anhydrous magnesium sulphate (0.5g, 4.15 mmol) was dissolved in 20 ml THF. The solution was cooled to 0°C. To this solution DIPEA (0.603ml, 3.362mmol) and aminoethyl morpholine (304 mg, 2.335 mmol) were added and the solution was stirred for 4 to 6 hrs. Control was performed by ³¹P NMR for peak at 68 ppm. After completion of the reaction solvent was evaporated under vacuum and solid residue was extracted with DCM (100 ml) and 20% potassium carbonate solution in water (100ml). The organic layer was dried over sodium sulphate and evaporated under reduced pressure. The residue was again dissolved in 10 ml of THF and precipitated in 100 ml pentane. The mixture was stirred for 2hs and then filtered under argon. The resulting white powder was dried under vacuum to obtain the desired product as white powder (0.46g, 0.027mmol) in 64.8% yield.

³¹P NMR (161 MHz, CDCl₃) δ = 68.42 (s), 62.79 (s), 62.56 (s), 8.11 (s). ¹H NMR (300 MHz, CDCl₃) δ = 7.73-7.65 (m, 54 H), 7.59 (d, J = 9.0 Hz, 48 H), 7.47(s, 24H), 7.24-7.18 (m, 72 H), 7.03-7.02 (m, 12 H), 3.96-3.89 (m, 48H), 3.65 (s, 192 H), 3.32 (d, J = 1.2 Hz, 54H), 3.16-2.99 (m, 176 H), 2.63-2.47 (m, 288H), ¹³C NMR: 151.34 (d), 150.69 (d), 139.00 (d), 135.73 (d), 133.06 (s), 128.37 (s), 127.55 (s), 121.80 (s), 121.67 (d), 66.86 (s), 58.63 (d), 53.35 (s), 37.39 (s), 33.05 (d), 30.89 (d).

General procedure for synthesis of cationic surface: Dendrimer G3 with amine on surface was dissolved on dry THF. Diethylether hydrogenchloride solution 1M (exactly 48 mol eq. of HCl) was added slowly at 0°C. After addition stirred at RT upto completion, after completion filtered under argon and dried in high vacuum to get white powder.

Supplementary table

Table S1. Primer sequences used for the RT-qPCR analyses

Target	Primer sequences	
	Forward	Reverse
RPLP2	5'-GCTGTGGCTGTTTCTGCTTC-3'	5'-ATGTCGTCATCCGACTCCTC-3'
Gus	5'-AGTTGTGTGGGTGAATGGGA-3'	5'-GGAAGGGTATGAGGGGTCAG-3'
TNF- α	5'-TGCCTATGTCTCAGCCTCTTC-3'	5'-GGTCTGGGCCATAGAACTGA-3'

Supplementary Figures

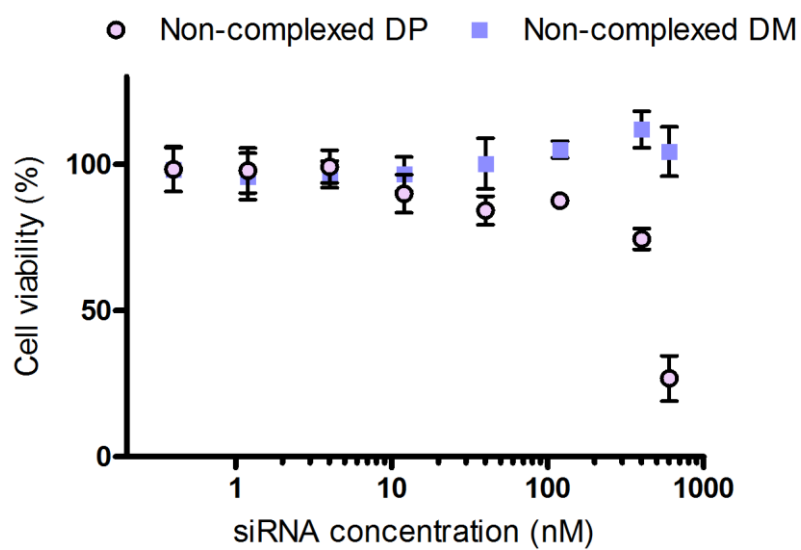


Figure S1. Cell viability of RAW264.7 cells after 24 h incubation with non-complexed DM and DP dendrimers measured using the MTT assay.

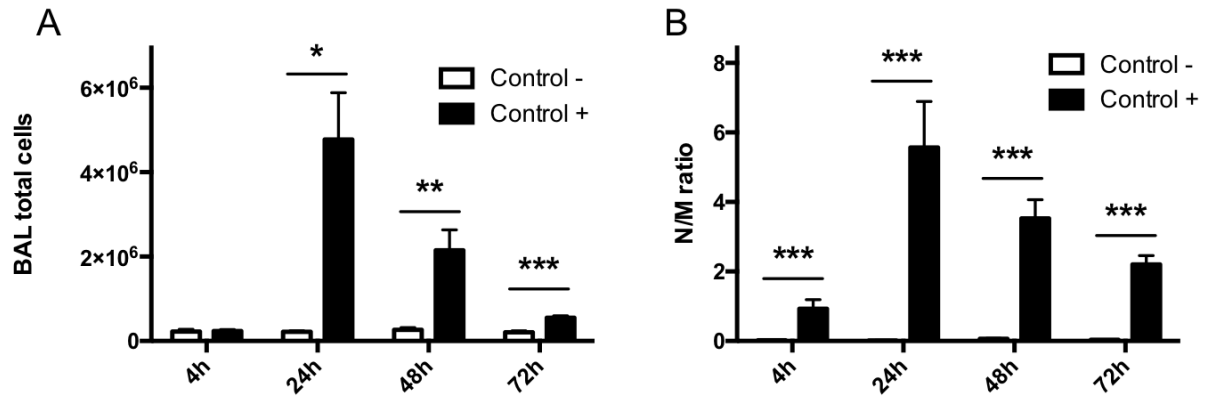


Figure S2. BAL cell count (A) and neutrophil-to-macrophage (N/M) ratio (B) of mice challenged with PBS (Control -) and mice challenged with LPS (Control +).

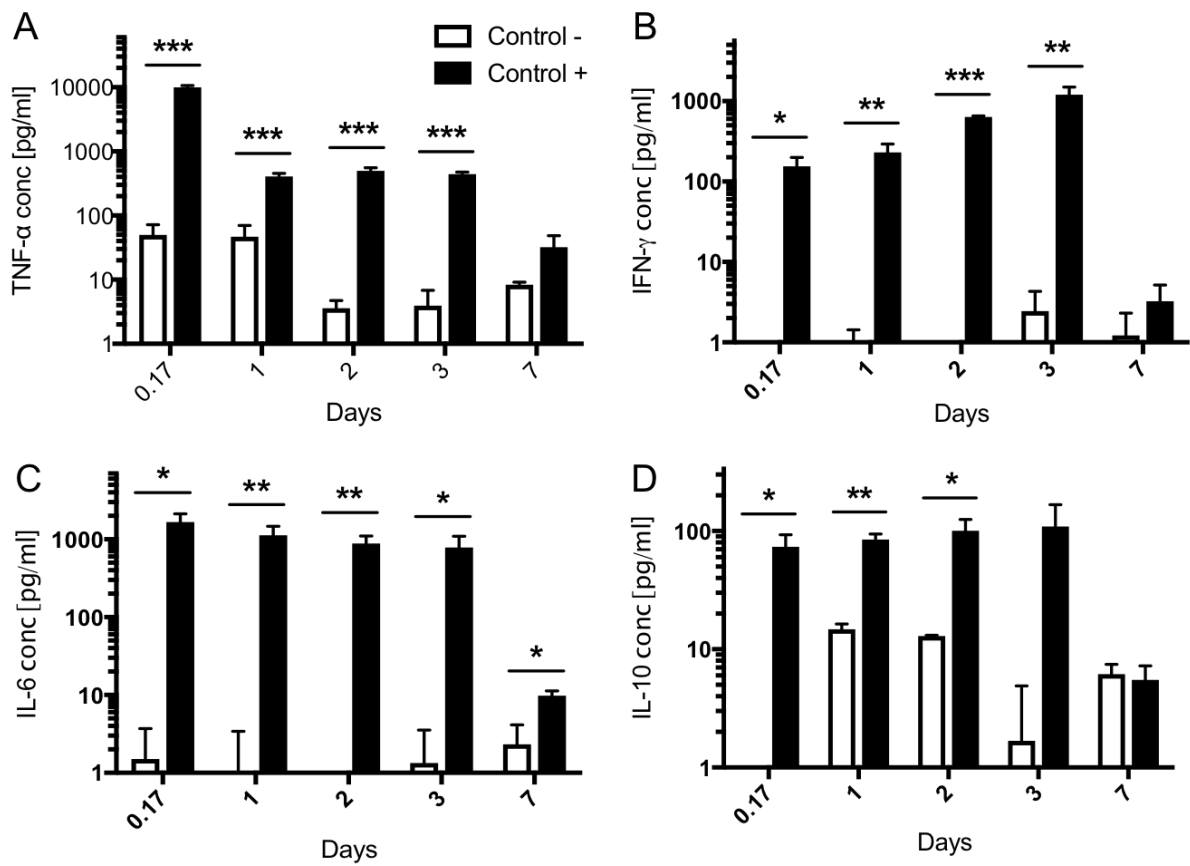


Figure S3. Cytokine concentrations in bronchoalveolar lavage of mice challenged with LPS (control +) and untreated mice (control -).

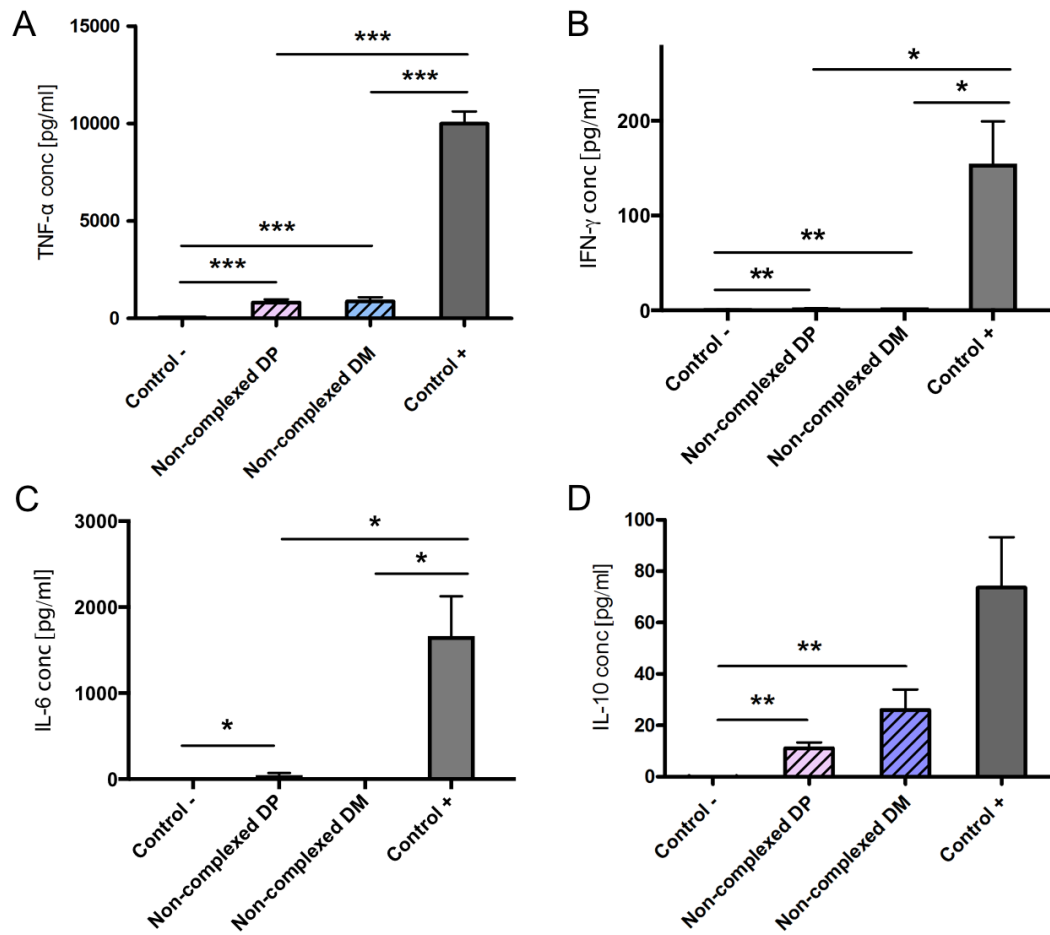


Figure S4. Cytokine concentrations in BAL of mice treated with LPS (Control +), mice treated with non-complexed dendrimers and untreated mice (Control -), 4h after administration of LPS/PBS.

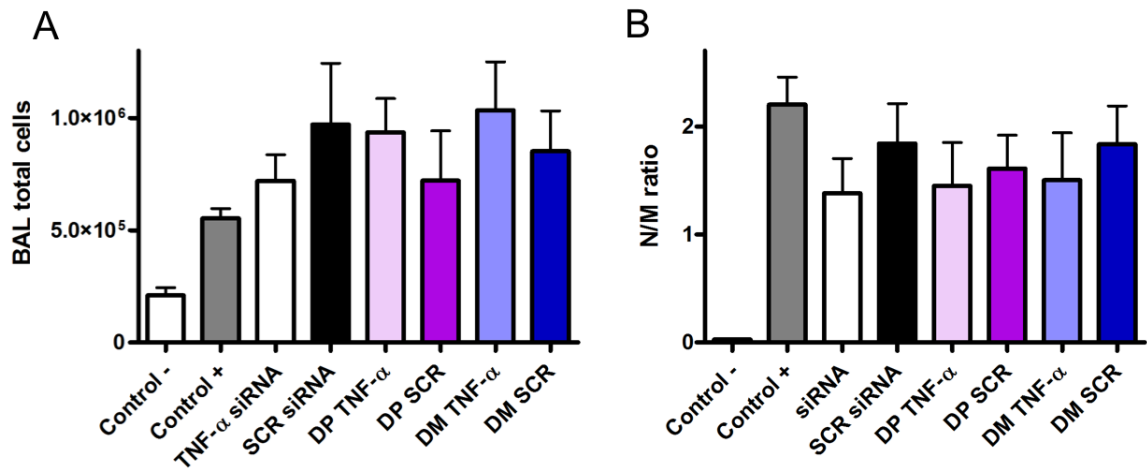


Figure S5. Total cell count (A) and neutrophil/macrophage (N/M) ratio (B) of the bronchoalveolar lavage (BAL) 72h after LPS challenge.

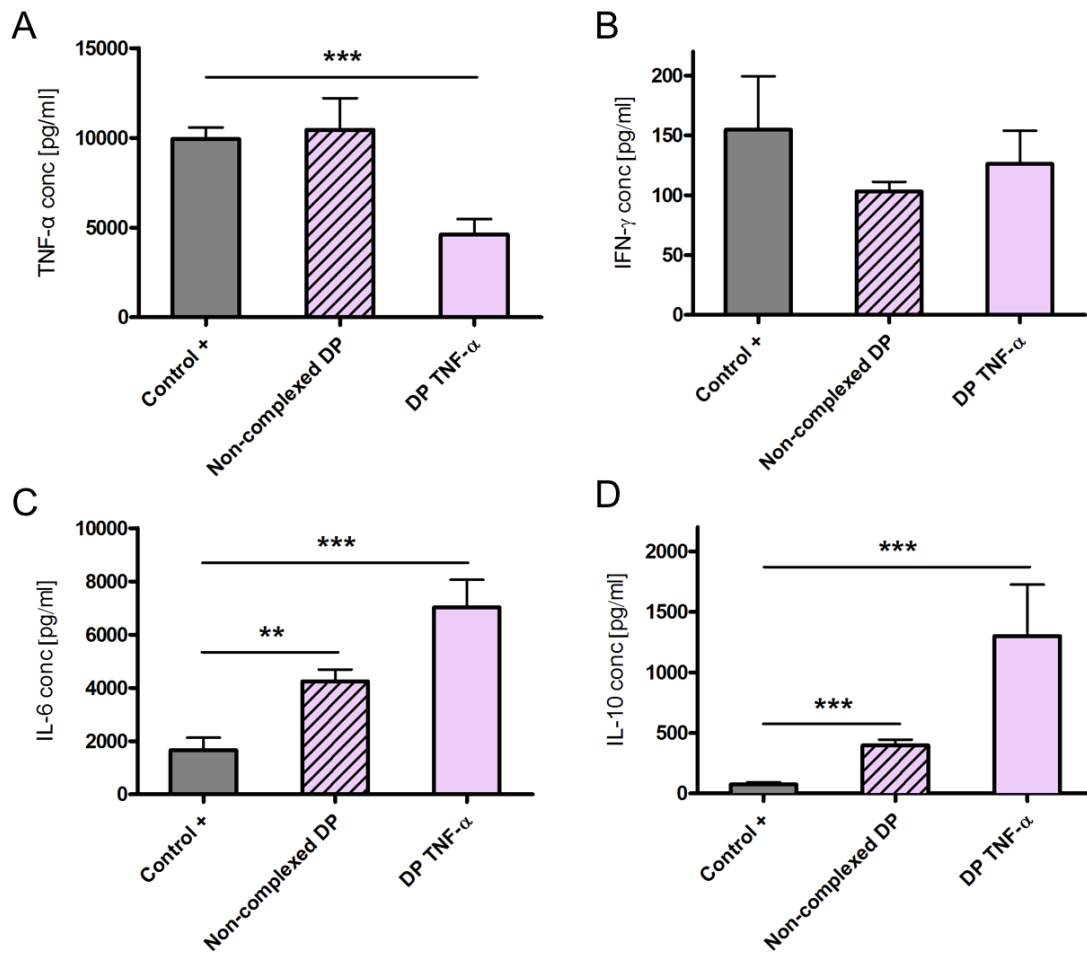


Figure S6. Cytokine concentrations in bronchoalveolar lavage of mice challenged with LPS (Control +) with pre-treatment of non-complexed DP dendrimer or DP TNF- α siRNA dendriplexes. BAL was taken 4h after LPS challenge.