

Supplemental Figure Legends

Supplemental Figure 1. Sorting of urine-infiltrating monocytic cells during BCG therapy. Lin^{neg}CD14⁺CD33⁺HLADR^{low} (red) and Lin^{neg}CD14⁺CD33⁺HLADR^{high} (grey) were FACS-sorted from post-BCG urine samples. The panels show overlay of both cell subsets after sorting (purity is indicated) from 1 representative sample out of 7.

Supplemental Figure 2. Bladder cancer cells and BCG induce monocytic MDSC *in-vitro*. PBMC from healthy donors (at least five per conditions) were co-cultured for 4 days with Bu68.8 or T24 cells (A), or with BCG at 3 different doses (MOI 0.05, 0.5 and 5) (B) and the effects of *Salmonella enterica* serovar Typhi strain Ty21a and heat-killed BCG (30min at 85°C) were compared to live BCG (MOI=0.5) (C). Graphs show the percentage of M-MDSC (Lin^{neg}CD14⁺CD33⁺CD11b⁺HLA-DR^{low} cells) in indicated conditions compared to medium only. **One-way ANOVAs followed by Dunnett's (A,B) or Tukey's (C) tests:** * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001. (D) PBMCs were co-cultured with indicated cell lines for 4 days; CD14⁺ cells were then sorted and subsequently co-cultured with autologous CFSE-labeled T cells (3-day stimulation with anti-CD3/CD28). Proliferation profiles are depicted in histograms of CFSE fluorescence intensity in indicated T-cell populations from 1 representative donor out of 4. Div: % cells with at least one division; PI: Proliferation Index.

Supplemental Figure 3. Recurrence-free and progression-free survivals. Recurrence-free (A) and progression-free (B) survivals were assessed using the Kaplan-Meier approach in the cohort of 28 patients receiving BCG therapy (with the first instillation at month 0 and the last at month 1.5). Censored patients are represented by tick marks.

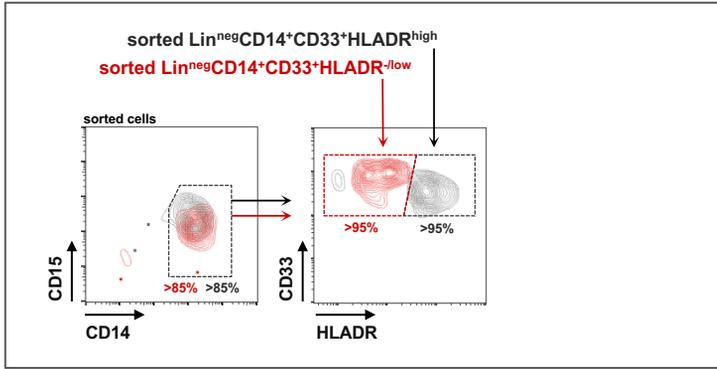
Supplemental Figure 4. Th1/Th2 profiles of urine-infiltrating CD4 T cells during BCG therapy. (A-B) CD4 T cells were expanded *ex-vivo* from twelve urine samples from patients with high (T/M^{high}, n=6) or low (T/M^{low}, n=6) T/MDSC ratio. (A) CXCR3 and CRTH2 expression in *ex vivo*-expanded CD4 T cells. (B) Th1 cytokines (IFN- γ , IL-2, TNF- α) and Th2 cytokines (IL-4 and IL-5) were measured in the supernatants of activated *ex vivo*-expanded CD4 T cells from urine samples and a “Th2 versus Th1” score was calculated (see methods section) for each sample. (C) IDO activity as assessed by the Kynurenins-to-Tryptophan (K/T) ratio in urine samples from patients of the T/M^{high} (n=9) and T/M^{low} (n=9) groups. Two-sided t-tests: *p<0.05.

Supplemental Figure 5. Induction of ILC2 by different bacteria. PBMC from 3 healthy donors were co-cultured with *Salmonella enterica* serovar Typhi strain Ty21a or with heat-killed or live BCG (MOI=1) for 4 days. Graph shows the percentage of ILC2 among ILC. **One-way ANOVA followed by Tukey's test:** *p<0.05; ** p<0.01; *** p<0.001.

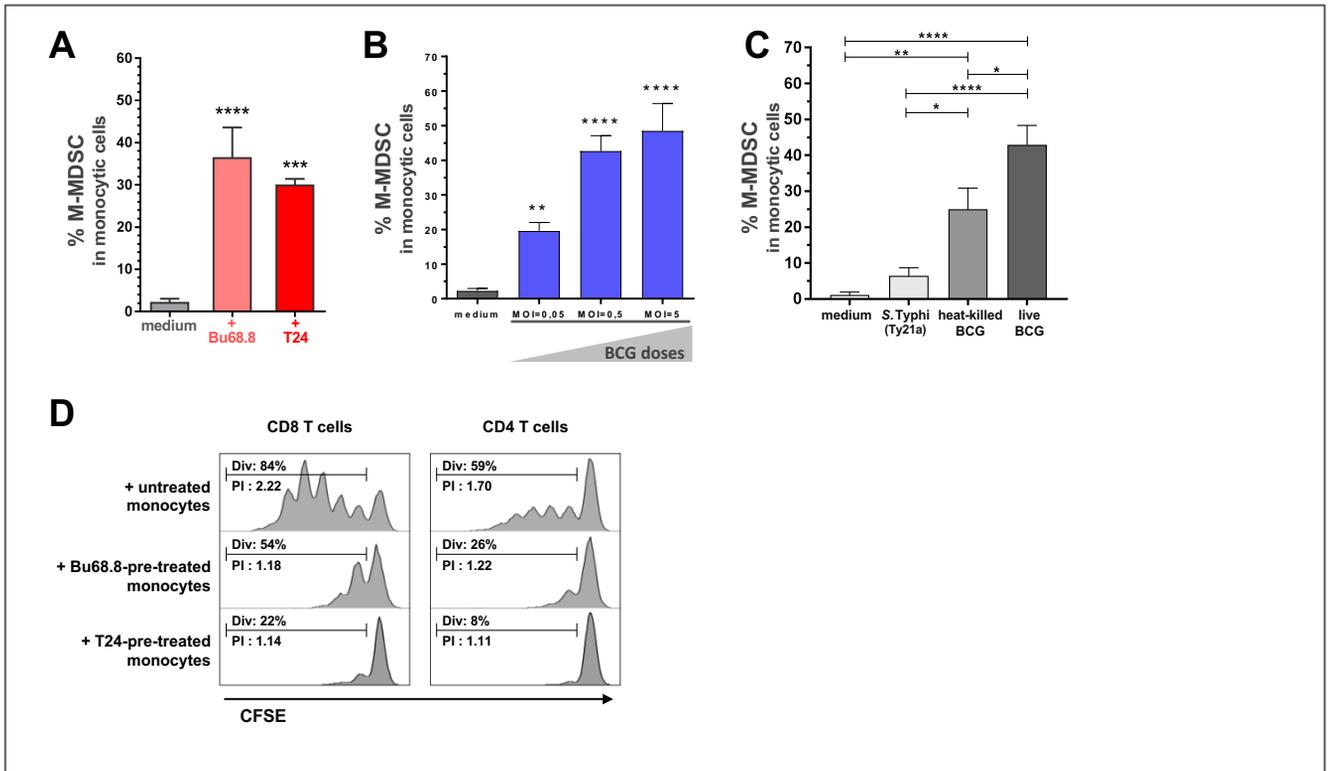
Supplemental Figure 6. Expression of CCR4 in peripheral and urine ILC from NMIBC patients and production of PGD2 by tumor cell lines. (A) *Ex-vivo* expression of CCR4 on peripheral ILC1 (Lin^{neg}CD127⁺CRTH2^{neg}c-Kit^{neg}), ILC2 (Lin^{neg}CD127⁺CRTH2⁺) and ILC3 (Lin^{neg}CD127⁺CRTH2^{neg}c-Kit⁺) from patients with non-muscle invasive bladder cancer (NMIBC; n=10) (**one-way ANOVA followed by Tukey's test:** *p<0.05; **** p<0.0001). (B) CCR4 expression in ILCs from 3 urine samples during BCG therapy. (C) Detection of PGD2 in the supernatants of indicated bladder tumor cell lines (biological duplicates) in the presence or absence of 30 μ M arachidonic acid (AA) as substrate (dashed line indicates limit of detection).

Supplemental Figure 7. Phenotypic analysis of IL-13 treated sorted monocytes. Sorted CD14⁺ cells from PBMC of HD (n=4) were cultured for 4 days with or without recombinant IL-13 (100ng.mL⁻¹). (A) Representative FACS-histograms showing HLA-DR expression in indicated conditions. (B) HLA-DR expression density (geometric mean fluorescence intensity, MFI) and frequency of HLA-DR^{low} in CD14⁺ cells. (C) Expression levels of various monocytes/macrophages markers on HLA-DR^{low} and HLA-DR^{high} CD14⁺ cells treated or not with IL-13. (D) Relative expression of Arginase-1, iNOS and C/EBP β transcripts by qPCR in CD14⁺ cells treated or not with IL-13. (E) Corresponding supernatants were harvested and soluble markers were measured by multiplex assay. Two-sided paired t-tests (B,D,E) or **one-way ANOVAs followed by Tukey's tests** (C). * p<0.05; ** p<0.01, **** p<0.0001.

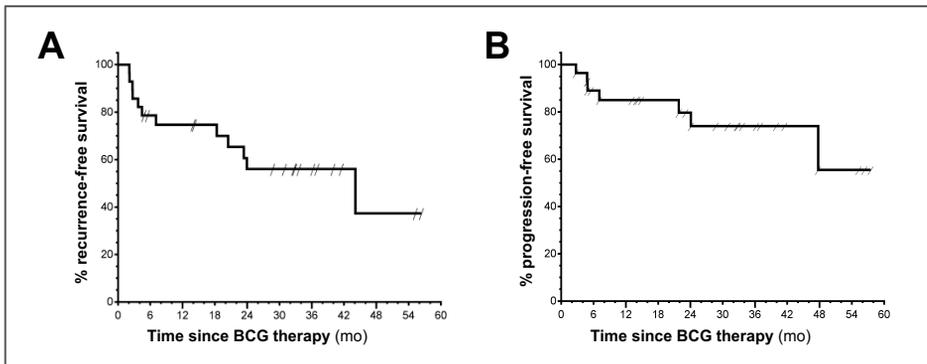
Supplemental Figure 1.



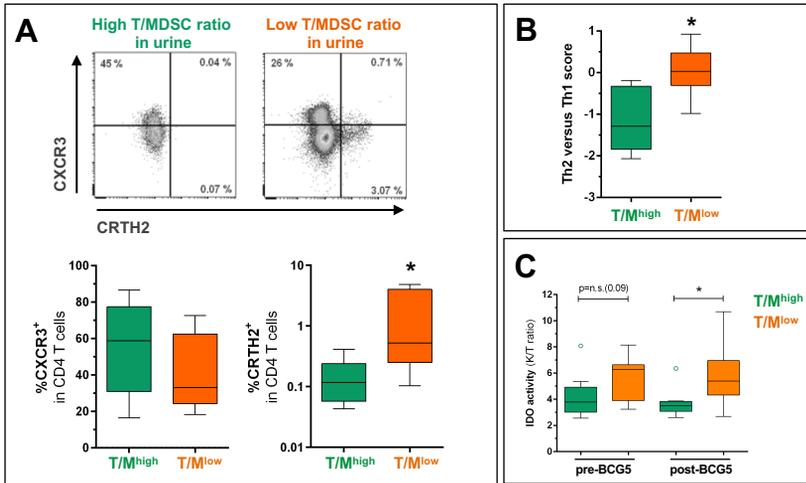
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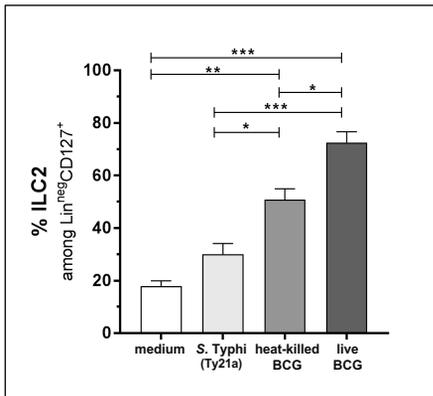
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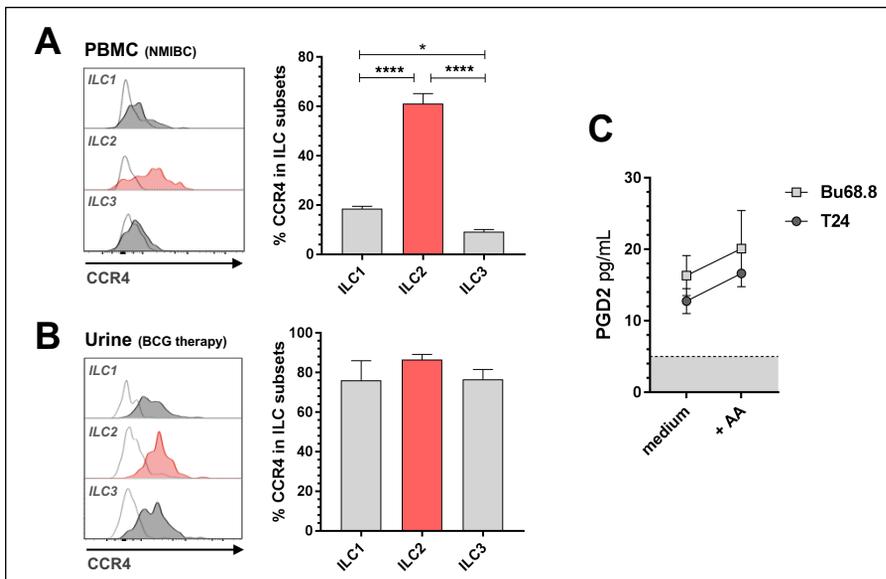
Supplemental Figure 4.



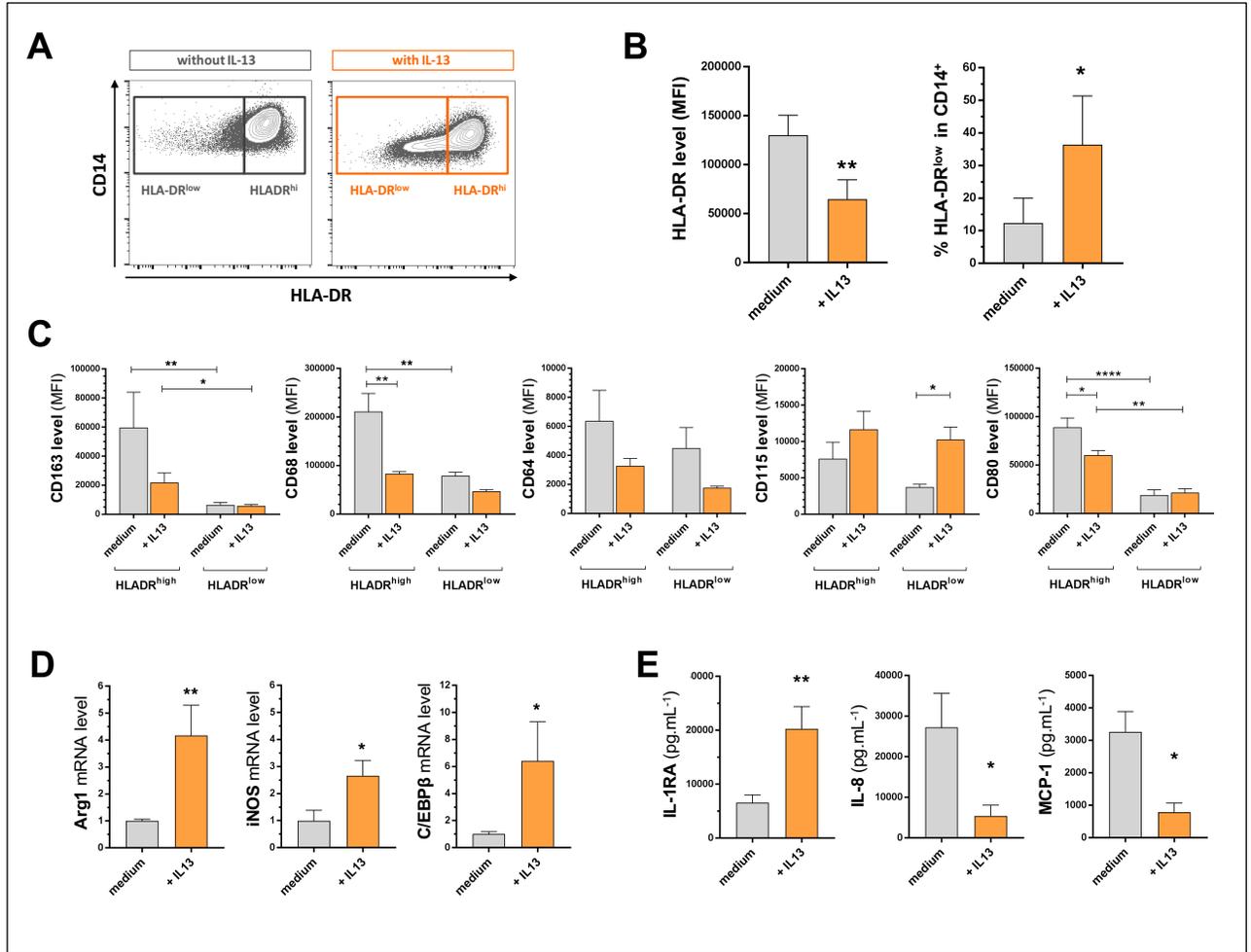
Supplemental Figure 5.



Supplemental Figure 6.



Supplemental Figure 7



Supplementary Table 1. Characteristics of MIBC patients

Characteristics	All patients
N° of patients	23
Age, yr, median (IQR)	71 (65-805)
Sex, n	
Male	18
Female	5
Tumor status, n (%)	
pT2	6 (26.1)
pT3	14 (60.9)
pT4	3 (13)
Draining lymph node status, n (%)	
Nx	5 (21.7)
N0	10 (43.5)
N1	4 (17.4)
N2	4 (17.4)
Neoadjuvant chemotherapy	10 (43.5)