

Supplemental Text

Table 1. Patient characteristics

	MGUS (n=9)	SMM (n=7)	MM (n=10)
Median age at diagnosis (min-max)	57 (41-80)	64 (34-71)	62 (51-79)
Race			
Caucasian	89% (8)	86% (6)	90% (9)
African American	0% (0)	14% (1)	10% (1)
unknown	11% (1)	0% (0)	0% (0)
Gender			
Male	55% (5)	29% (2)	90% (9)

Table 2. Cosine similarity between scRNA seq data and flow cytometry results

	MGUS	SMM	MM	all
B	0.91	0.93	0.99	0.90
T	0.97	0.99	0.99	0.98
NK	0.86	0.79	0.92	0.80
Mono	0.95	0.97	0.99	0.96

Table 3. Cell proportions per sample in each disease stage

MGUS

	MGUS_115821	MGUS_110071	MGUS_110858	MGUS_111326	MGUS_111557	MGUS_111889	MGUS_115131	MGUS_116169	MGUS_117111
CD14 Mono	18.9	19.2	11.6	15.6	18.3	12	23.2	20.4	22.3
CD8 Memory_2	36.1	23.3	3.6	5.9	23.8	10.9	5.8	8.7	5.8
CD4 Memory	22.9	17.7	31	22.5	16.4	30.7	28	28.8	7.9
CD16 Mono	5.8	1.6	4.6	1.2	4.6	2	7.2	1.2	0.4
CD4 Naive	0.8	1.6	3.5	17.8	0.9	14.8	2.2	1.3	0.3
Naive B	2.2	2.8	6.7	4.2	3.8	2.5	4.8	4.7	0.2
NK	3.3	7.6	10.7	6	7.2	7	7	7.6	1.5
Prog_B 1	0.4	0.1	2.6	0.9	2.8	0.4	0.7	2.6	1.1
Treg	1.3	0.2	0.7	0.4	0.2	0.3	0.4	0.5	0
Prog_DC	0.1	0.1	0.6	0.8	0.1	0	0.3	0.3	0.3
CD8 Effector_1	1.2	7.4	0.6	3.4	6.4	2.8	0.2	2	1.4
CD8 Effector_2	3.3	2.9	1.2	1.4	1.5	0	2.8	3.3	21.6
CD8 Memory_1	0.3	0.7	0.1	0.4	0.1	0	0.3	0.3	0.6
GMP	1	2.1	2.3	1.7	3.4	0.9	3.1	5.5	16.3
Prog_B 2	0.8	0	1.3	0.2	0.6	0.1	0.7	0.6	0.3
Memory B	0.3	0.8	3.1	0.7	1.5	3.7	2.8	0.9	2.9
CD56 bright NK	0.3	0.3	0.1	1.9	0.3	0.3	0.5	0.1	0.1
Prog_Mk	0.5	0.6	0.5	0.2	0.2	0.6	0.6	0.9	1.3
CD8 Naive	0.1	6.9	6.4	8.6	1.1	9.3	2.2	7.7	0.2
cDC2	0.1	0	2	1.2	0.1	0.1	1.3	0.5	1.9
pDC	0.2	0.4	0.4	0.6	0.8	0.5	0.1	0.9	4.9
HSC	0.1	0.8	1	0.2	1	0	0	0.8	6.4
LMPP	0	0	0.1	0.3	0.1	0	0.1	0.2	0.2
MAIT	0	2.6	5	3.8	3.1	0.6	4.7	0.2	1.9
gdT	0	0.3	0.3	0.1	1.7	0.4	1	0.1	0.2

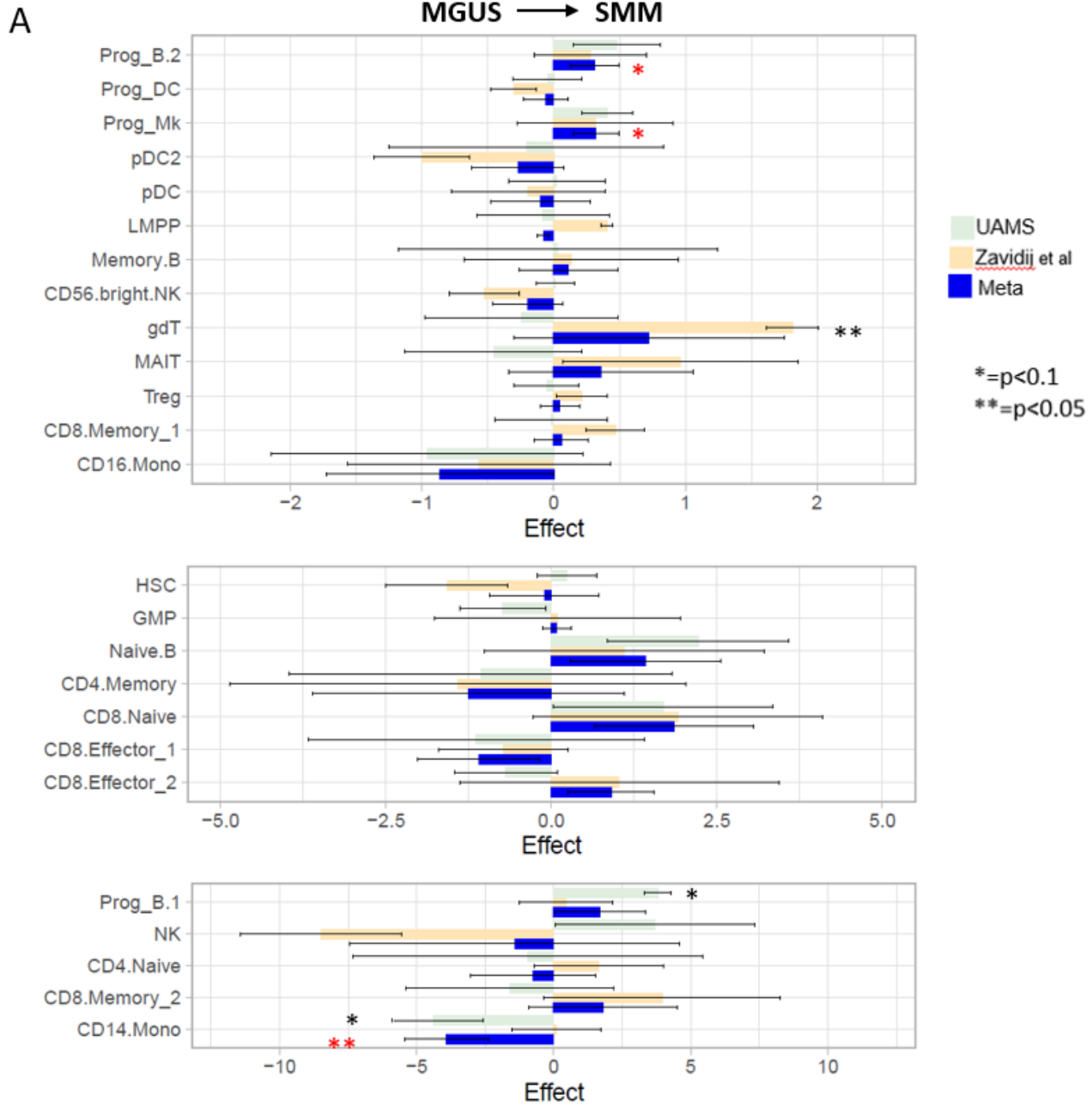
SMM

	SMM_108615	SMM_109248	SMM_110101	SMM_112168	SMM_112288	SMM_119207	SMM_84857
CD14 Mono	11.2	12.3	16.7	15.4	11.7	15.4	12.2
CD8 Memory_2	12.6	23.5	14.3	6.9	9.9	7.5	10.3
CD4 Memory	27.2	14.1	32	19.8	21.5	20.5	17.1
CD16 Mono	1.6	2.9	1.3	1.9	5.4	1.9	0.5
CD4 Naive	5.3	7.6	4.6	3.4	1.9	3.6	1.1
Naive B	4.2	2.2	1.1	4.5	14.2	1.8	12.4
NK	4.2	6.1	8.5	5.3	20.1	21.4	5.2
Prog_B 1	2.2	8.3	0.1	12.2	1.7	3.5	7.7
Treg	0.5	0	0.6	1	0.6	0.2	0
Prog_DC	0.3	1.1	0	0.3	0	0	0
CD8 Effector_1	1.8	0	3.3	2.5	1.1	2.1	1.1
CD8 Effector_2	2.8	4	0.2	5.1	1.3	3.3	8.1
CD8 Memory_1	1.5	0	0	0	0.1	0.2	0
GMP	2.7	6.1	0	4.5	0.4	3.5	5.8
Prog_B 2	0.2	1.8	0.1	3	0.3	0.5	1.1
Memory B	2.3	0.4	1	0	5.6	1.4	2.5
CD56 bright NK	0.2	0	1.4	0.3	0.5	0.7	0
Prog_Mk	0.1	0.4	1.3	0.2	0.4	0.4	4.5
CD8 Naive	14.4	5.4	9.9	8.5	0.3	3.8	3
cDC2	0.8	0	0.3	0	0.4	1.7	1.1
pDC	0.4	0.7	0.1	1.9	0.4	1.4	2.1
HSC	0.5	3.2	0	1	0.3	0.3	4.1
LMPP	0	0	0	0.3	0	0	0
MAIT	2.3	0	2.8	1.7	1.9	4.8	0.1
gdT	0.4	0	0.4	0.3	0	0.1	0.1

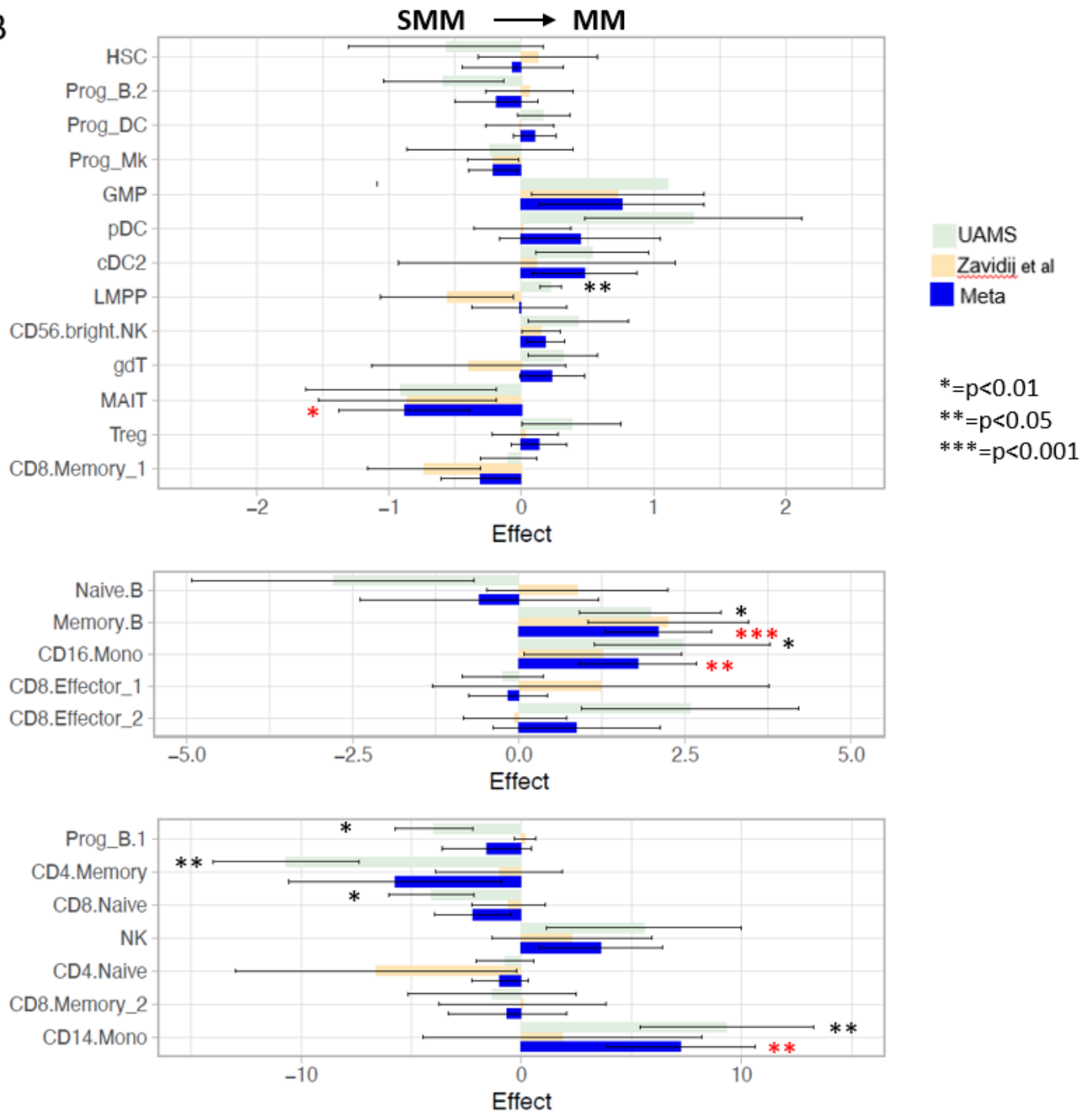
MM

	MM_100742	MM_101011	MM_107404	MM_113436	P06	P04	P05	P03	P01	P02
CD14 Mono	23.5	18.1	16	22.4	29.7	20.8	7.8	12.1	51.8	27.6
CD8 Memory_2	2.1	3.1	12.6	6.1	3.4	29.6	8.1	19.4	0.9	23
CD4 Memory	25.3	19.4	7.2	11.3	5.5	4.4	17.1	8.8	8.8	2.1
CD16 Mono	7.3	2.5	0.2	0.4	4.7	11	3.8	1.2	9.2	6.4
CD4 Naive	1.7	7.5	5.1	0.8	7.6	0.8	7.2	0.8	0.1	0.2
Naive B	0	6.2	3.5	1.1	4.5	4	3	0.8	5.2	1.4
NK	22.5	12.9	1.1	4	17.6	13.7	31	34.3	7.1	12.7
Prog_B 1	0	3.6	1.9	5	0.5	0	0	0	0.4	0
Treg	2.8	0.4	0	0.1	0.5	0.7	0.5	0.6	0.1	1.1
Prog_DC	0.3	0.4	1.2	0.8	0.8	0	0.1	0	0.4	0.1
CD8 Effector_1	0	1.4	0.8	0.1	1.3	3.3	1.6	2	0.2	4.3
CD8 Effector_2	3.1	3.1	14	8	4.9	2.2	4.2	11.7	2.1	7.7
CD8 Memory_1	0	0.2	0.3	0.6	0	0.2	0.1	0.1	0	0
GMP	1.4	6.4	8.8	20.3	3.9	1	0.3	0.2	1	0.5
Prog_B 2	0	0.7	1	1.9	0.1	0	0	0	0.3	0
Memory B	2.4	0.5	6.6	0.7	2.6	5	7	2.8	3.8	7.5
CD56 bright NK	3.5	0.1	0.1	0	0.2	1	1.1	1.7	1	0.2
Prog_Mk	2.1	0.6	0.4	0.6	0.2	0.3	0.5	0.5	0.4	2.3
CD8 Naive	1.4	2.6	6.5	1.3	5.3	0	3.1	1.3	1.4	0.2
cDC2	0	0.7	3.2	2.6	1.6	0.6	0.4	0	1.8	0.5
pDC	0.3	1.5	5	7.4	4	0.6	1.7	0	2.1	0.4
HSC	0	1.4	2	3.7	0.1	0.1	0.1	0.2	0	0.4
LMPP	0.3	0.4	0.6	0.6	0.1	0	0.1	0	0	0.4
MAIT	0	3.7	2	0.1	0.7	0.6	0.8	0.3	1.2	1
gdT	0	2.5	0	0	0	0.2	0.2	1.2	1	0

Figure 1. Quantitative alterations of distinct cell subsets from progression of monoclonal gammopathy of undetermined significance (MGUS) to smoldering MM (SMM) (A), SMM to MM (B) and MGUS to advanced stages (ADV= SMM and MM, C) and precursor stages (MGUS/SMM) to newly diagnosed MM (NDMM) in each dataset and the combined data. Significance is shown in black asterisks for the single datasets and in red for the combined dataset.

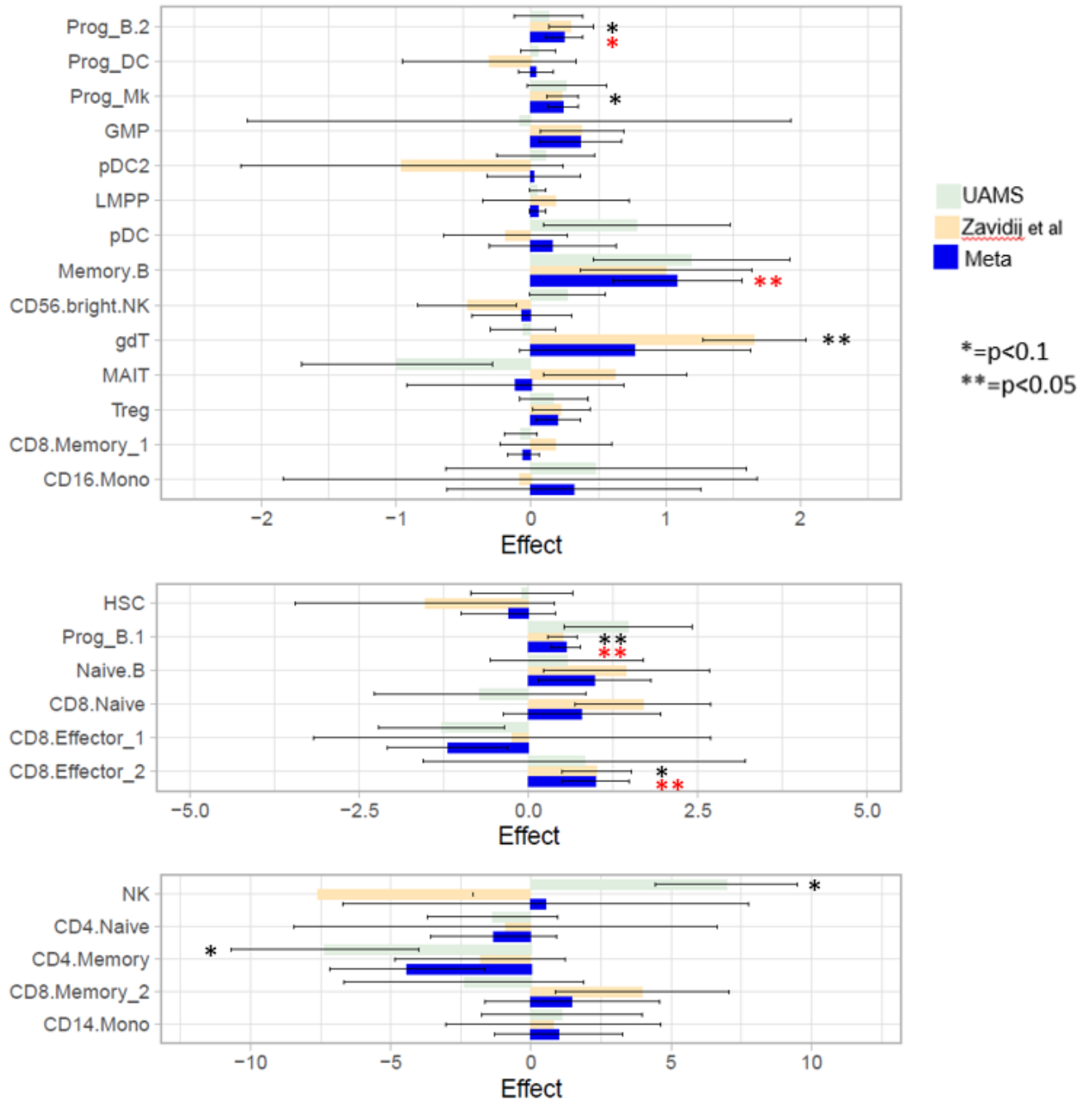


B



C

MGUS → SMM/MM



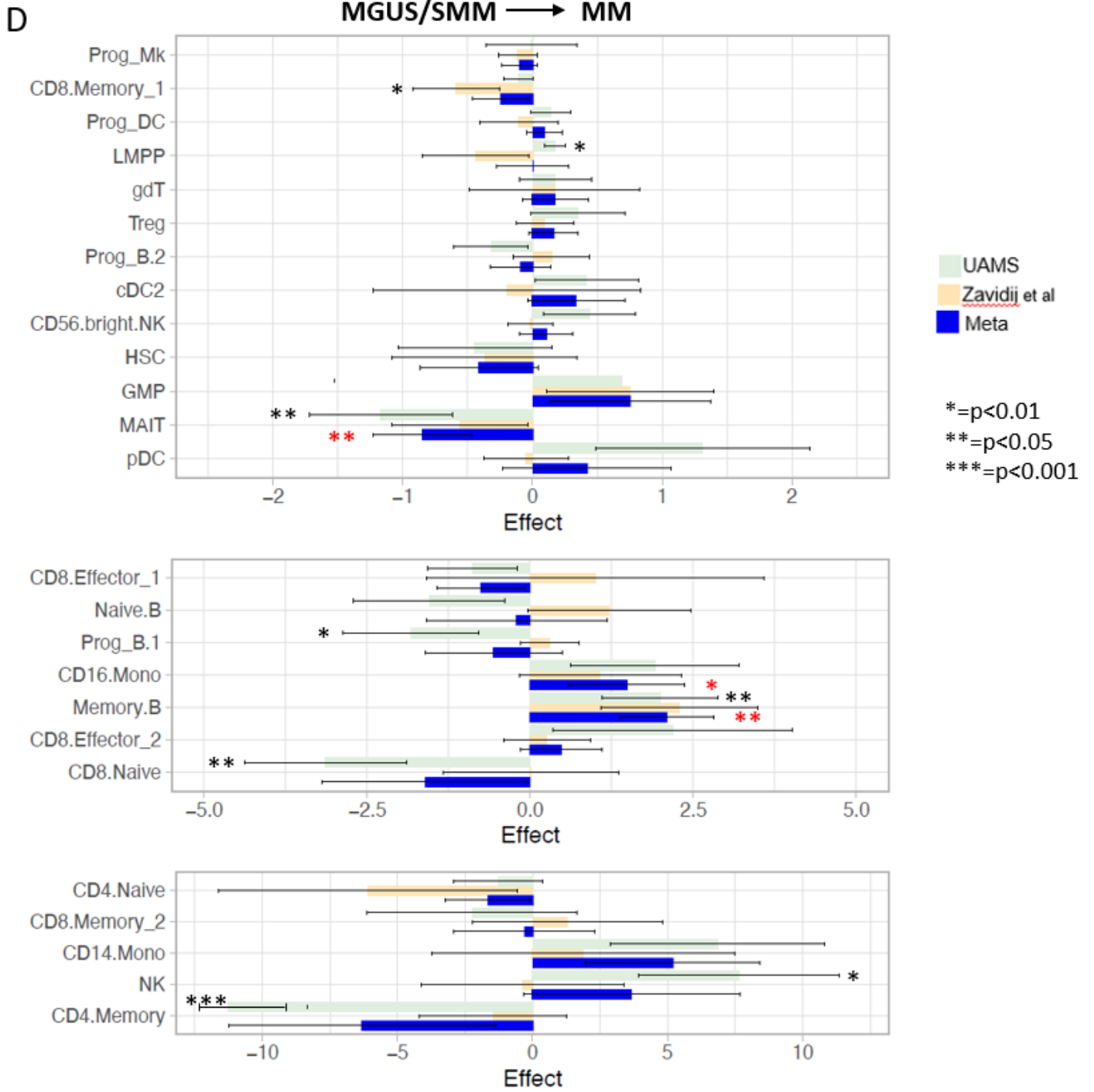


Figure 2. Heatmap of cell subset expression for each individual patient. Samples from the external dataset are annotated by disease stage_extern and followed by the ID from the original manuscript.

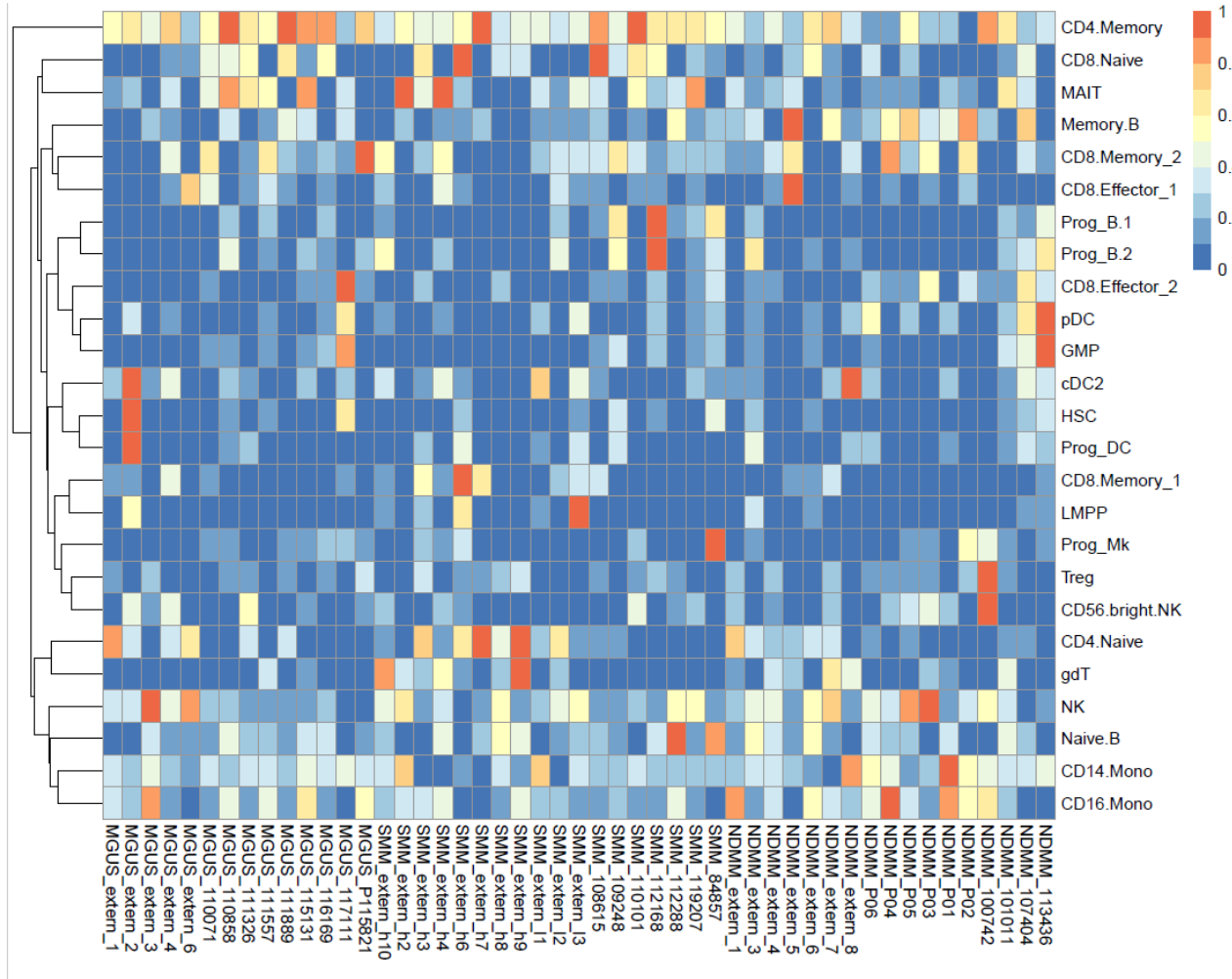


Figure 3. Proportion of B cells (A), T cells (B), CD56 NK cells (C) and monocytes in the BM aspirate by 8-color flow cytometry.

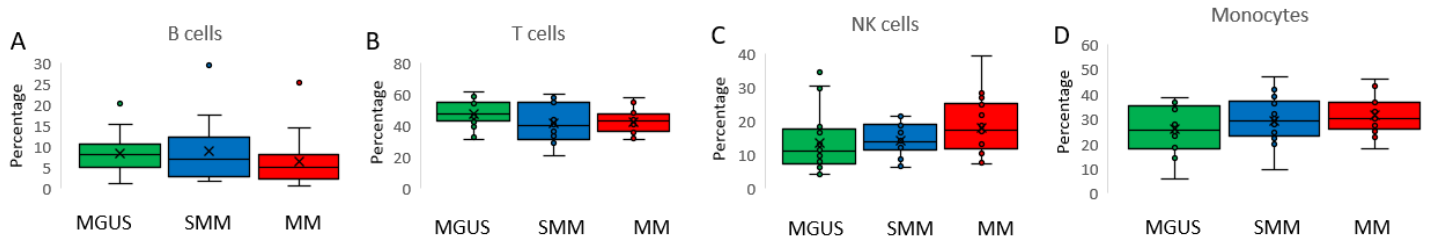


Figure 4. Proportion of CD4 T cells (A), CD8 T cells (B) and CD56 NK cells (C) in the peripheral blood by disease stage. Fig

