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Supplementary information

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Fecal microbiota transplantation plus immunotherapy in non-small cell lung cancer and melanoma: the phase 2 FMT-LUMINate trial

In the format provided by the authors and unedited

Supplemental Table 1: Donor Demographics

Donor ID	Age	Sex	BMI	Ethnicity
D1	37	M	22.3	Caucasian
D2	28	M	27.5	Caucasian
D5	37	M	21.8	Asian
D7	27	M	21.8	Caucasian
D9	44	F	21.3	Caucasian
D10	37	M	22.3	Caucasian
D11	36	M	29.4	Caucasian
D13	21	M	22.9	Caucasian
D14	39	F	19.6	Caucasian
D15	24	M	24.3	African

Supplemental Table 2: Information on myocarditis cases

Patient ID	Age[a]	Sex	Diagnosis	Donor	AE onset timing (days)[b]	AE grade	Clinical details	Treatment	Best response	Patient status
101-003[c]	40	Male	Cutaneous melanoma	D5	22	3	Troponin[d] 599 ng/L LVEF[e] 53%	Methylprednisolone Prednisone	PR	Death due to disease progression
102-014[c]	76	Male	Cutaneous melanoma	D5	25	4	Troponin[d] 11969.9 ng/L LVEF[e] difficult to assess but globally decreased	Methylprednisolone Infliximab Plasmapheresis Prednisone	PR	Alive
106-001[c]	51	Female	Cutaneous melanoma	D9	205	3	Troponin levels not available[d] LVEF[e] 20% Normal angiography	Prednisone	CR	Alive

[a] *Age at the time of enrollment*
[b] *Relative to first cycle of ICI*
[c] *Patient 101-003 experienced co-existing immune-related adverse events: grade 1 fatigue, grade 2 thyroiditis, grade 2 pneumonitis. Patient 102-014 experienced co-existing grade 4 myositis overlap syndrome. Patient 106-001 experienced co-existing immune-related adverse events of grade 1 dry mouth.*
[d] *Troponin peak during myocarditis diagnosis*
[e] *Left ventricular ejection fraction at the time of myocarditis diagnosis*

Supplemental Table 3

REAGENT	SOURCE	IDENTIFIER
LIVE/DEAD™ Fixable Blue Dead Cell Stain	Invitrogen™	Cat. No. L23105
BD Horizon™ Brilliant Stain Buffer Plus	BD Biosciences	Cat. No. 566385
Brilliant Violet 510™ Streptavidin	BioLegend	Cat. No. 405233
BV605 Mouse Anti-Human CD194	BD Biosciences	Cat. No. 562906, RRID:AB_2737882
BUV661 Mouse Anti-Human CD196 (CCR6)	BD Biosciences	Cat. No. 750696, RRID:AB_2874817
BUV737 Mouse Anti-Human CCR7 (CD197)	BD Biosciences	Cat. No. 749676; RRID:AB_2873937
PE/Dazzle™ 594 anti-human CD199 (CCR9) Antibody	BioLegend	Cat. No. 358918, RRID:AB_2715935
Brilliant Violet 570™ anti-mouse/human CD11b Antibody	BioLegend	Cat. No. 101233, RRID:AB_10896949
Alexa Fluor® 647 anti-human CD123 Antibody	BioLegend	Cat. No. 306024, RRID:AB_2562070
R718 Mouse Anti-Human CD127	BD Biosciences	Cat. No. 566967, RRID:AB_2869977
Spark Blue™ 550 anti-human CD14 Antibody	BioLegend	Cat. No. 367148, RRID:AB_2832724
Brilliant Violet 421™ anti-human CD141 (Thrombomodulin) Antibody	BioLegend	Cat. No. 344114, RRID:AB_2563858
BUV805 Mouse Anti-Human CD16	BD Biosciences	Cat. No. 748850, RRID:AB_2873253
APC anti-human CD163 Antibody	BioLegend	Cat. No. 333610, RRID:AB_2074533
BB515 Mouse Anti-Human Siglec-1 (CD169)	BD Biosciences	Cat. No. 565353, RRID:AB_2739204
PE/Fire™ 640 anti-human CD19 Antibody	BioLegend	Cat. No. 302274, RRID:AB_2860773
BV480 Mouse Anti-Human CD1c	BD Biosciences	Cat. No. 746677, RRID:AB_2743949
PerCP/Cyanine5.5 anti-human CD206 (MMR) Antibody	BioLegend	Cat. No. 321122, RRID:AB_10899411
PE/Fire™ 700 anti-human CD25 Antibody	BioLegend	Cat. No. 356145, RRID:AB_2876678
Brilliant Violet 650™ anti-human CD3 Antibody	BioLegend	Cat. No. 300468, RRID:AB_2629574
PE anti-human CD301 (CLEC10A) Antibody	BioLegend	Cat. No. 354704, RRID:AB_11219002

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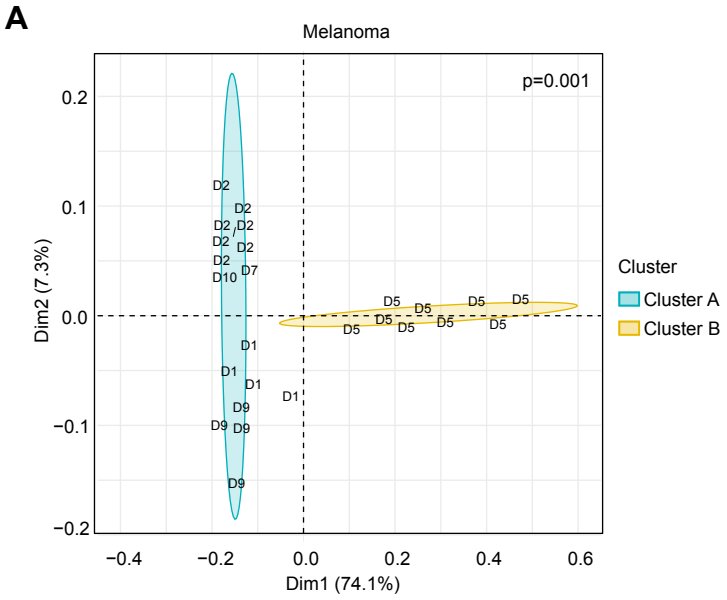
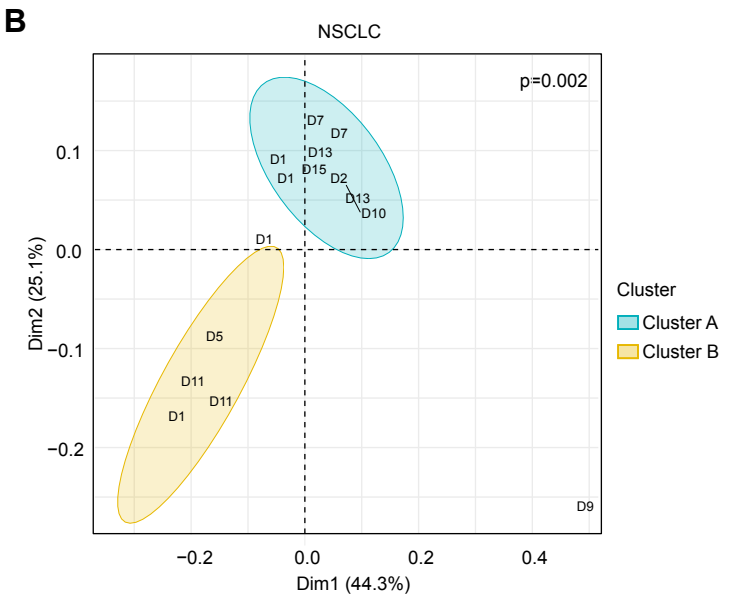
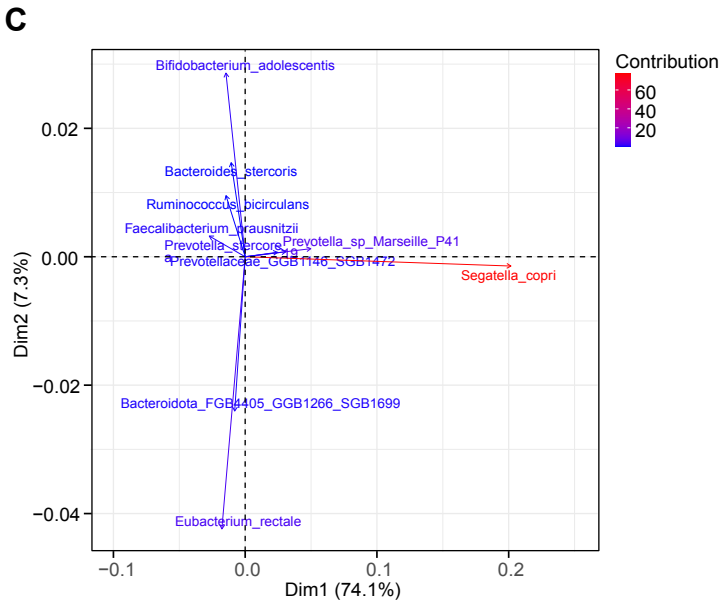
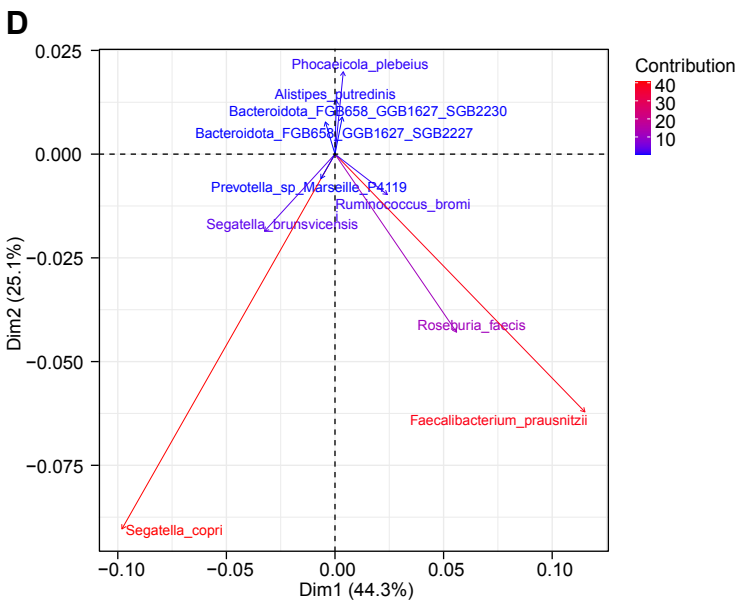
cFluor YG584 Anti-Human CD4	Cytek Biosciences	Cat. No. R7-20041, RRID:AB_2885083
Brilliant Violet 650™ anti-human CD40 Antibody	BioLegend	Cat. No. 334338, RRID:AB_2566209
PerCP anti-human CD45 Antibody	BioLegend	Cat. No. 368506, RRID:AB_2566358
BUV395 Mouse Anti-Human CD45RA	BD Biosciences	Cat. No. 740298, RRID:AB_2740037
BUV563 Mouse Anti-Human CD5	BD Biosciences	Cat. No. 741354, RRID:AB_2870855
Spark NIR™ 685 anti-human CD69 Antibody	BioLegend	Cat. No. 310957; RRID:AB_2888776
APC/Fire™ 810 anti-human CD8 Antibody	BioLegend	Cat. No. 344764, RRID:AB_2860890
BV786 Mouse Anti-Human CD86	BD Biosciences	Cat. No. 740990, RRID:AB_2870657
APC/Fire™ 750 anti-human CD88 (C5aR) Antibody	BioLegend	Cat. No. 344316, RRID:AB_2750445
BUV496 Mouse Anti-Human CD89	BD Biosciences	Cat. No. 750617, RRID:AB_2874749
CD152 (CTLA-4) Monoclonal Antibody (14D3), PerCP-eFluor™ 710	Thermo Fisher Scientific	Cat. No. 46-1529-42, RRID:AB_2573718
PE-Cy™7 Mouse Anti-Human CD183	BD Biosciences	Cat. No. 560831, RRID:AB_2033944
BUV615 Rat Anti-Human CXCR5 (CD185)	BD Biosciences	Cat. No. 751293, RRID:AB_2875306
BV711 Mouse Anti-Human FcεR1α	BD Biosciences	Cat. No. 747783, RRID:AB_2872247
PE/Fire™ 810 anti-human HLA-DR Antibody	BioLegend	Cat. No. 307683, RRID:AB_2904336
Human Integrin alpha 4 beta 7/LPAM-1 Alexa Fluor® 405 Antibody	R and D Systems	Cat. No. FAB10078V
BV750 Mouse Anti-Human CD279 (PD-1)	BD Biosciences	Cat. No. 747446, RRID:AB_2872125
CD274 (PD-L1, B7-H1) Monoclonal Antibody (MIH1), PE-Cyanine5	Thermo Fisher Scientific	Cat. No. 15-5983-42, RRID:AB_2802211
Slan (M-DC8) Antibody, anti-human, VioBlue®	Miltenyi Biotec	Cat. No. 130-119-868, RRID:AB_2751897

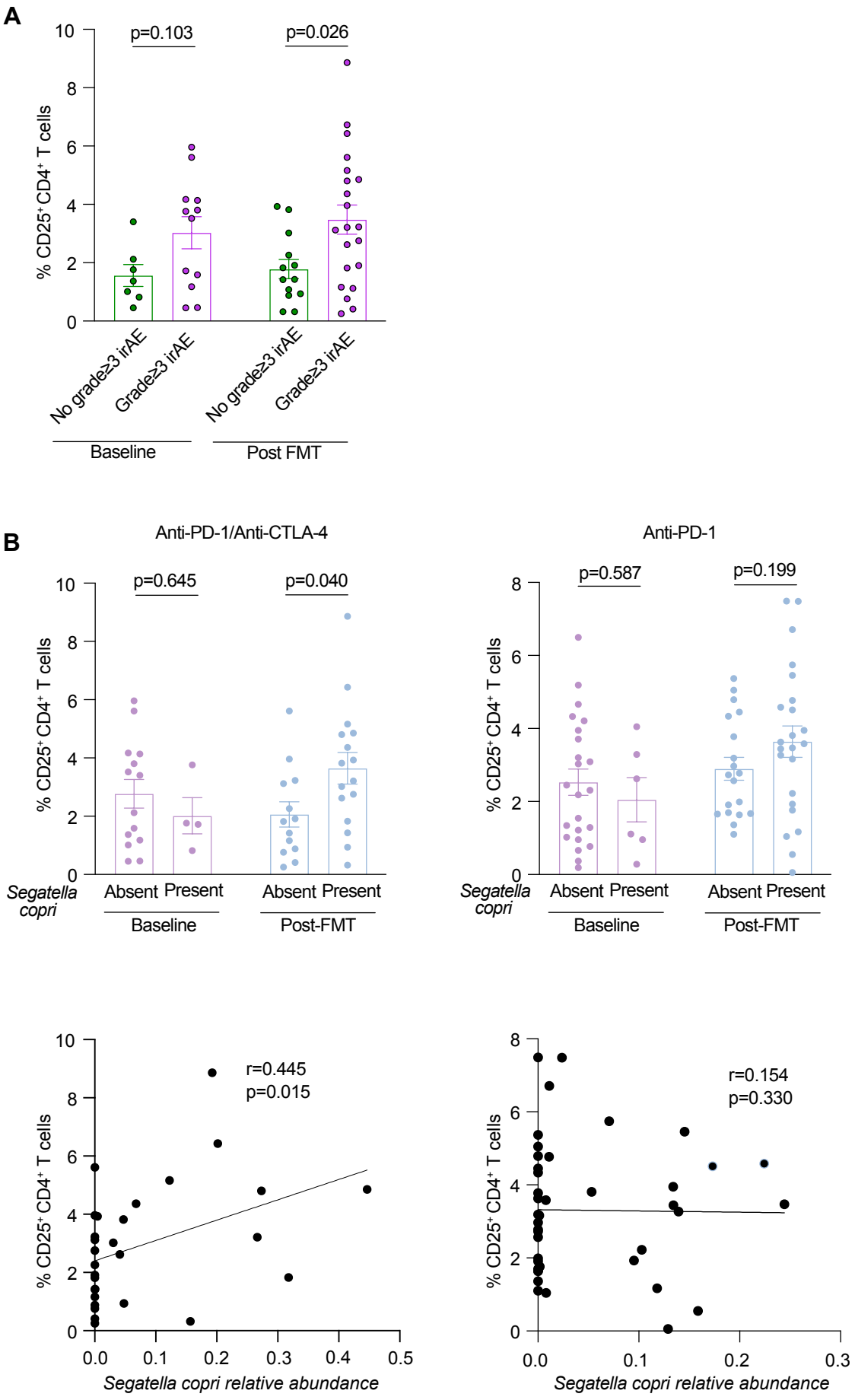




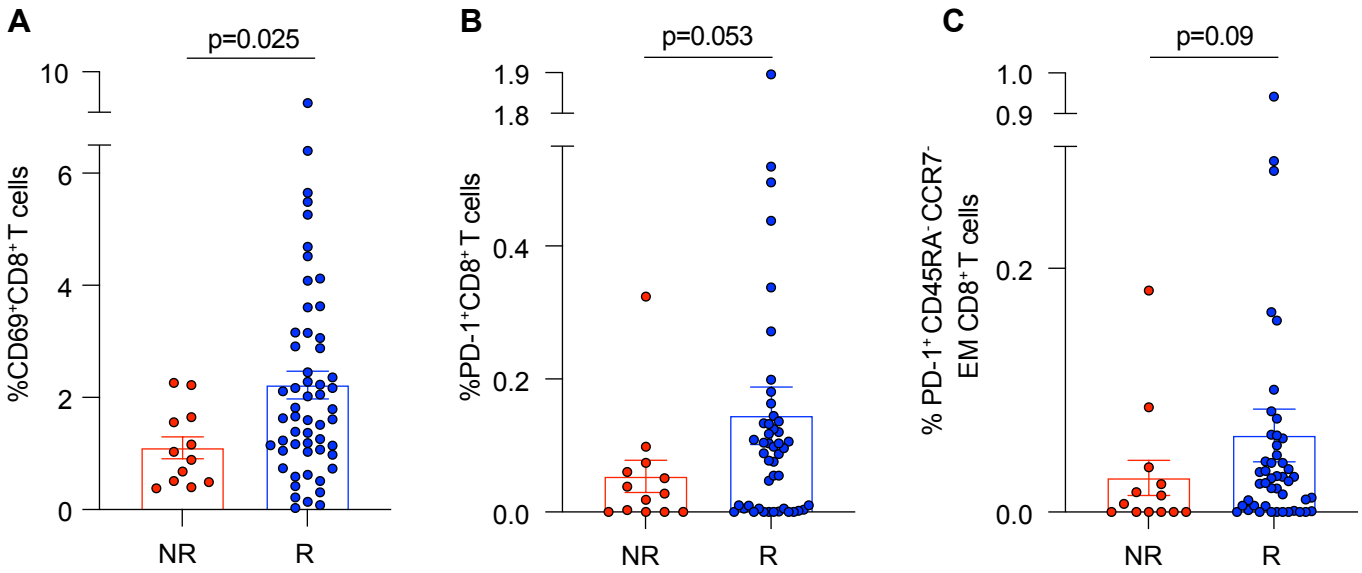




Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3

Supplementary figure legends

Supplementary Figure 1. Subgroup analysis of donor clusters. A. Unsupervised cluster analysis using shotgun metagenomic sequencing of healthy donors using Bray-Curtis index, group separation assessed using one-way PERMANOVA (two-tailed) for melanoma (n=26). **B.** Contribution of species driving donor clusters for melanoma; **C.** Unsupervised cluster analysis using shotgun metagenomic sequencing of healthy donors using Bray-Curtis index, group separation assessed using one-way PERMANOVA (two-tailed) for NSCLC (n=15). **D.** Contribution of species driving donor clusters for NSCLC.

Supplementary Figure 2. Association of S. copri engraftment and irAE development according to ICI backbone. A. Bar plots show the frequency of $CD25^{+}CD4^{+}$ T cells in peripheral blood from patients without (green) or with (purple) grade ≥3 irAE, measured at baseline and post-FMT, (n=7 for patients without grade ≥3 irAE and 13 for patients with grade ≥3 irAE at baseline; p=0.103 and n=12 for patients without grade ≥3 irAE and 21 for patients with grade ≥3 irAE post-FMT; p=0.026), p-value computed by non-parametric Mann Whitney U test (two-sided). Bars indicate mean ± SEM. **B.** Frequency of $CD25^{+}CD4^{+}$ T cells in patients receiving anti-PD-1/anti-CTLA-4 or anti-PD-1 alone, according to *S. copri* presence, at baseline and post-FMT and Spearman correlation between *S. copri* relative abundance and $CD25^{+}CD4^{+}$ T cell frequency in patients receiving anti-PD-1/anti-CTLA-4 or anti-PD-1 alone, post-FMT. For bar-plot representations (n=14 for baseline, *S. copri* absent in patients receiving anti-PD-1/anti-CTLA-4, 4 for baseline, *S. copri* present in patients receiving anti-PD-1/anti-CTLA-4; p=0.645, 13 for post-FMT, *S. copri* absent in patients receiving anti-PD-1/anti-CTLA-4, 16 for post-FMT, *S. copri* present in patients receiving anti-PD-1/anti-CTLA-4; p=0.040, 23 for baseline, *S. copri* absent in patients receiving anti-PD-1, 6 for baseline, *S. copri* present in patients receiving anti-PD-1; p=0.587, 19 for post-FMT, *S. copri* absent in patients receiving anti-PD-1, 23 for post-FMT, *S. copri* present in patients receiving anti-PD-1; p=0.199), p-value computed by non-parametric Mann Whitney U test (two-sided). Bars indicate mean ± SEM. For Spearman R correlation (two-sided), n=29 for post-FMT in patients receiving anti-PD-1/anti-CTLA-4 and 42 for post-FMT in patients receiving anti-PD-1.

Supplementary Figure 3. CD8 T cell subpopulations according to response status. A. n=55 for R and 12 for NR for $\%CD69^{+}CD8^{+}$ T cells **B.** n=46 for R and 13 for NR for $\%PD\text{-}1^{+}CD8^{+}$ T cells and **C.** n=46 for R and 13 for NR for $\%PD\text{-}1^{+}CD45RA^{-}CCR7^{-}$EM $CD8^{+}$ T cells. p-value computed by non-parametric Mann Whitney U test (two-sided). Bars indicate mean ± SEM. R; responder. NR; non-responder.