

Intra-tumoral microbes correlate with immune cell fractions in lung cancer biopsies

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Background

- Exogenous sequences in bacteria have been found in many tumors.
- Their effects on clinical outcomes remain largely unknown.
- We hypothesize that intratumoral microbes elicit effects through the recruitment of immune cells, such as CD8+ T-cells that are important for immunotherapy response.

Methods

- We obtained RNA-seq data from biopsies of 480 tumors (Melanoma=16, Gastrointestinal=104, p=20 Renal Cell Carcinoma=20, Sarcoma=118, Lung=202) from patients treated at The Ohio State University Comprehensive Cancer Center, as part of the Oncology Research Information Exchange Network (ORIEN) under the OSU Total Cancer Care Program (TCC)
- Reads aligned to human and exogenous genomes using TopHat2¹ and Kraken2/Bracken², respectively. Exogenous databases included bacteria, fungi, viruses, archaea and eukaryotes.
- Human gene expression was deconvolved to relative abundances of immune cells using CIBERSORT³. Across cancers, an average of 99.87% of reads were aligned to the human reference genome.
- The difference in the distribution of tumor infiltrated immune cells among different types of cancer was compared by using Kruskal-Wallis test.
- The correlation between relative abundances of microbes and immune cells in each cancer type was evaluated by Spearman correlation method.
- Data analyses were performed in R and SAS

Abbreviations
CUT: Melanoma
GI: Gastrointestinal
GU: Genitourinary
RCC: Renal Cell Carcinoma
SAR: Sarcoma
THO: Thoracic

Results

Figure 1. Comparisons of percent of tumor infiltrated immune cells between lung cancer and other cancers

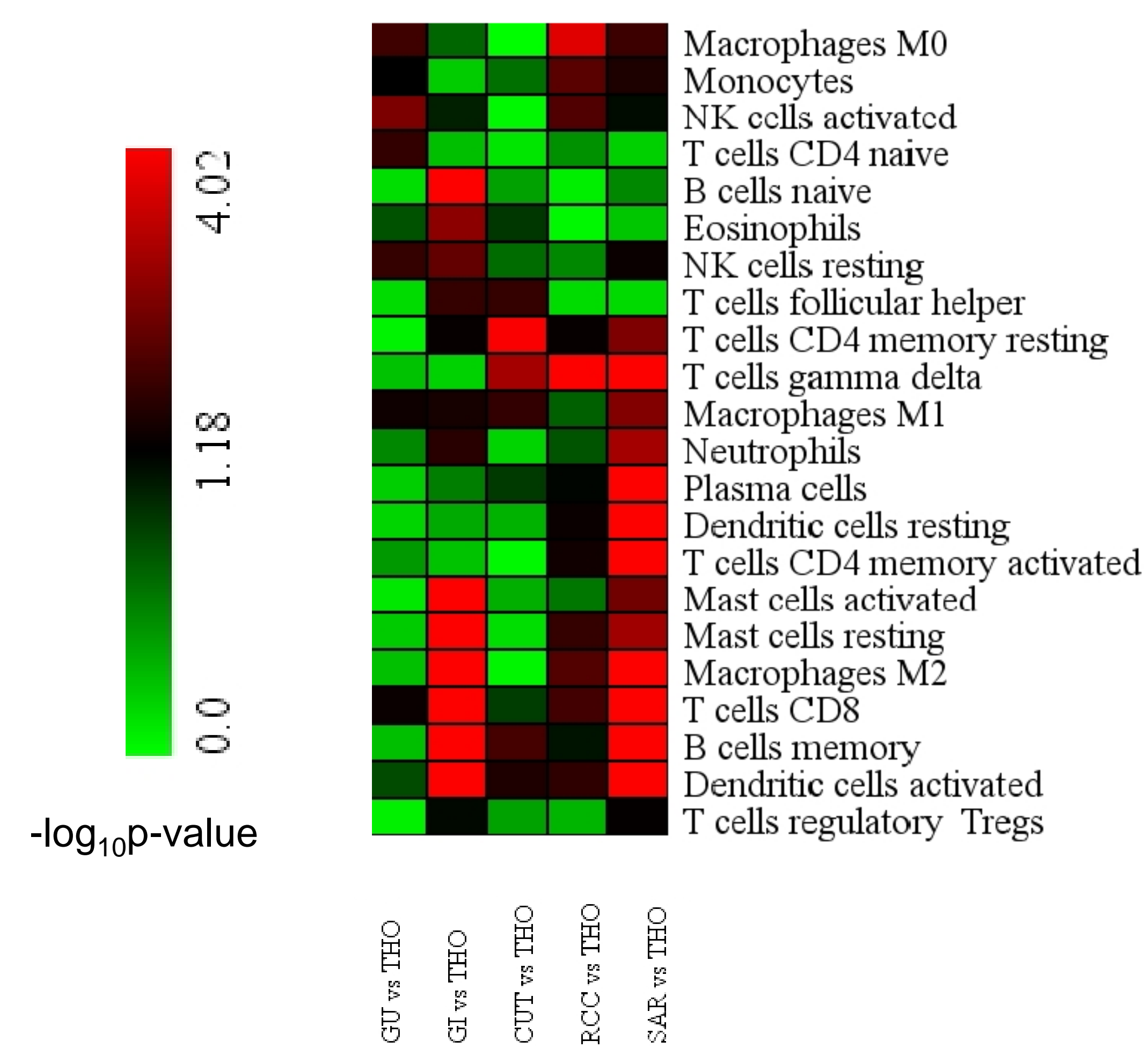


Table 1. Cohort summary

Covariates	Description	CUT	GI	GU	RCC	SAR	THO
Demographic	Age (std)	59 (10.78)	59 (11.72)	61 (12.22)	56 (11.68)	56 (15.99)	63 (10.04)
	BMI (std)	34 (8.72)	29 (6.18)	31 (8.98)	34 (7.68)	29 (6.03)	27 (5.82)
	Percent Male	0.75	0.6	0.8	0.75	0.53	0.53
	N	16	104	20	20	118	202
Treatment Type	Chemo	5	91	17	12	90	142
	Other	13	58	12	9	32	54
Stage	0A	0	0	3	0	0	0
	1A/1B	1	3	1	2	16	54
	2A/2B/2C	5	19	1	3	19	51
	3A/3B/3C	7	31	7	9	40	31
	4A/4B/4C	0	47	3	6	14	42
	Unknown	3	4	5	0	29	24

Figure 2. Tumor infiltrated immune cell distributions in cancer

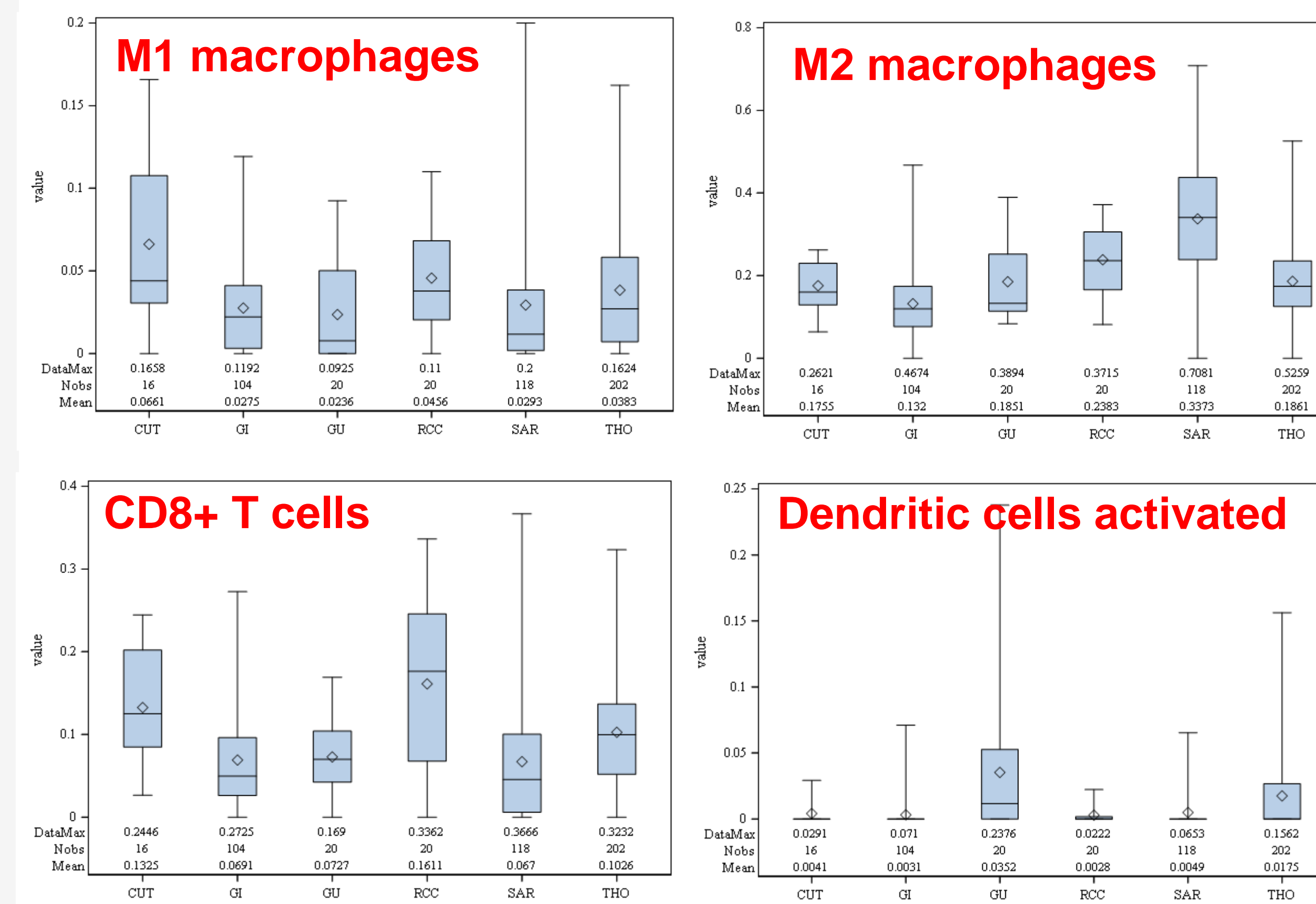
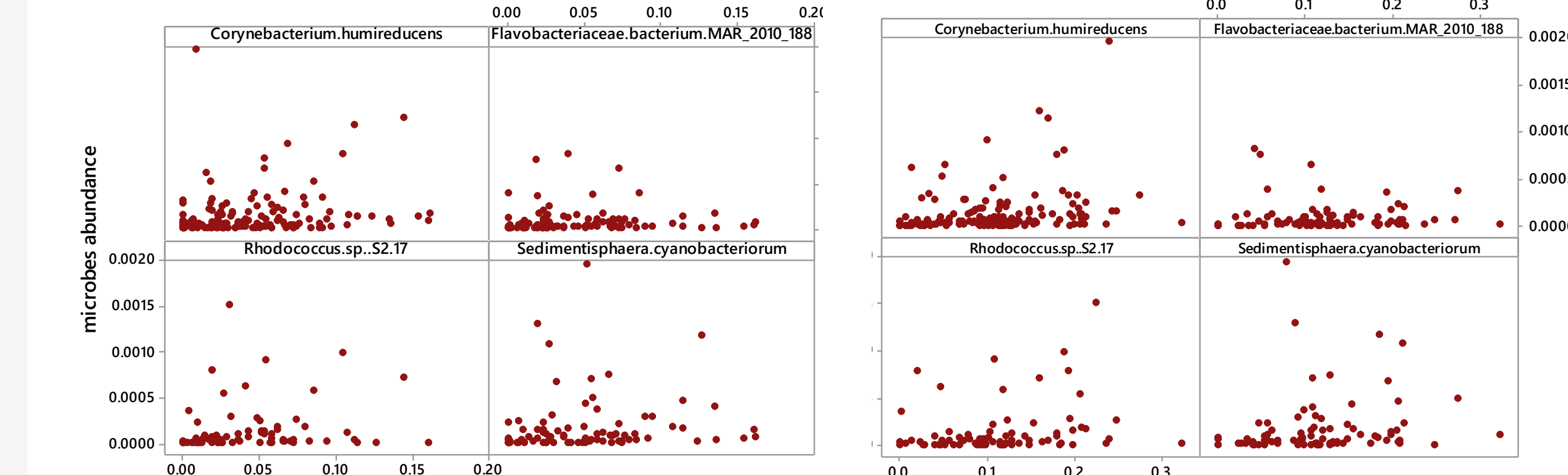


Table 2. Top 10 Taxon associated with M1 macrophages or CD8+ T cells

Taxon	Rho	p-value
Methylobacterium.sp._WL1	-0.28817	<.0001
Pseudomonas.lundensis	-0.27645	<.0001
Citrobacter.freundii	-0.26871	0.0001
Vibrio.cholerae	-0.25143	0.0003
Enterobacter.oligotrophica	-0.24375	0.0005
Thaueria.chlorobenzoica	0.28708	<.0001
Fabrizicola.sp._K13M18	0.28951	<.0001
Bacillus.megaterium	0.33116	<.0001
Sedimentisphaera.cyanobacterium	0.3358	<.0001
Corynebacterium.humireducens	0.41018	<.0001

Taxon	Rho	p-value
Actinomyces.sp._WMMB499	-0.23053	0.001
Herbaspirillum.robiniae	-0.21596	0.002
Bosea.vaviloviae	-0.20026	0.0043
Fabrizicola.sp._K13M18	0.21533	0.0021
Acinetobacter.pittii	0.22749	0.0011
Planococcus.sp._Y42	0.23073	0.001
Acinetobacter.juonii	0.24069	0.0036
Thaueria.chlorobenzoica	0.24481	0.0034
Flavobacteriaceae.bacterium.M	0.26709	0.0001
Corynebacterium.humireducens	0.27868	<.0001

Figure 3. The association between tumor infiltrated M1 macrophages, CD8+ T cells and microbes in lung cancer



Spearman correlation analysis showed that 4 microbes positively associated with both macrophages M1 and CD8+ T cells ($|r|>0.2$, p -value <0.05)

Conclusions

- The compositions of tumor infiltrated immune cells were different in other cancers compared with in lung cancer.
- CD8+ T-cells, M1 macrophages and the activated dendritic cells were significantly enriched in lung cancer (p -values <0.0001), and M2 macrophages were significantly enriched in sarcoma (p -values <0.0001).
- Corynebacterium.humireducens*, *Flavobacteriaceae.bacterium*, *Rhodococcus.sp._S2.17*, *Sedimentisphaera.cyanobacterium*, positively associated with both macrophages M1 and CD8+ T cells ($|r|>0.2$, p -value <0.05) in lung cancer.

Acknowledgements & References

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