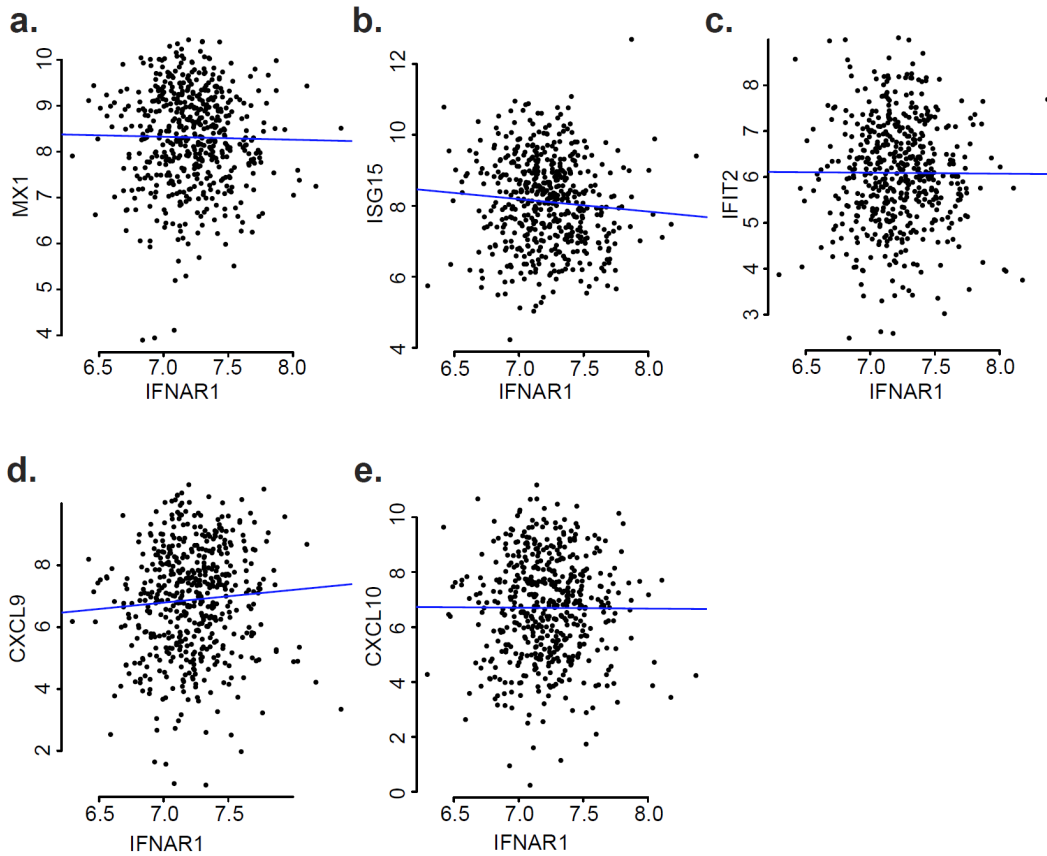1   **Supplementary Materials (Gong, Donnelly, Heath et al.):** Six supplementary figures and

2   three supplementary tables are provided for this manuscript.

3

4   **Supplementary Figure 1**

5

6   **Supplementary Figure 1. The expression levels of *IFNAR1* were not correlated with**

7   **interferon-stimulated genes in HNSCC specimens.** Spearman's correlation analysis was

8   performed to assess the relationship between the expression levels of *IFNAR1* and those of *MX1*

9   **(a)**, *ISG15* **(b)**, *IFIT2* **(c)**, *CXCL9* **(d)** and *CXCL10* **(e)** among 520 HNSCC specimens in the

10   TCGA database. Each dot represents one HNSCC specimen.

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Supplementary Figure 2
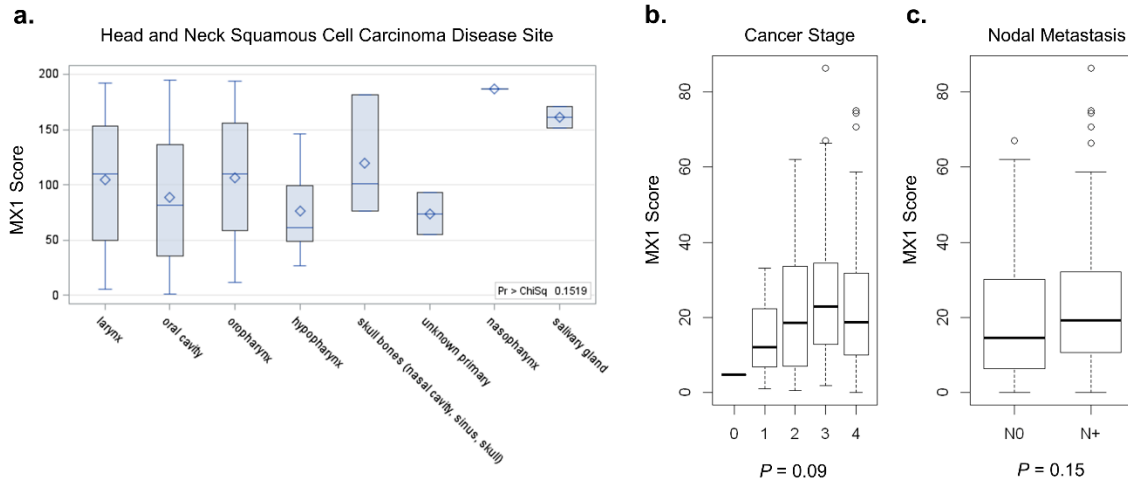
Supplementary Figure 2. Association of MX1 immunohistochemical scores with disease site, cancer stage, and nodal metastasis. Raw MX1 scores were generated by quantifying MX1 immunohistochemical staining in TMAs from 195 HNSCC patients, followed by correlation with primary disease site **(a)**, cancer stage **(b)**, or status of nodal metastasis **(c)**. No statistical differences were observed bet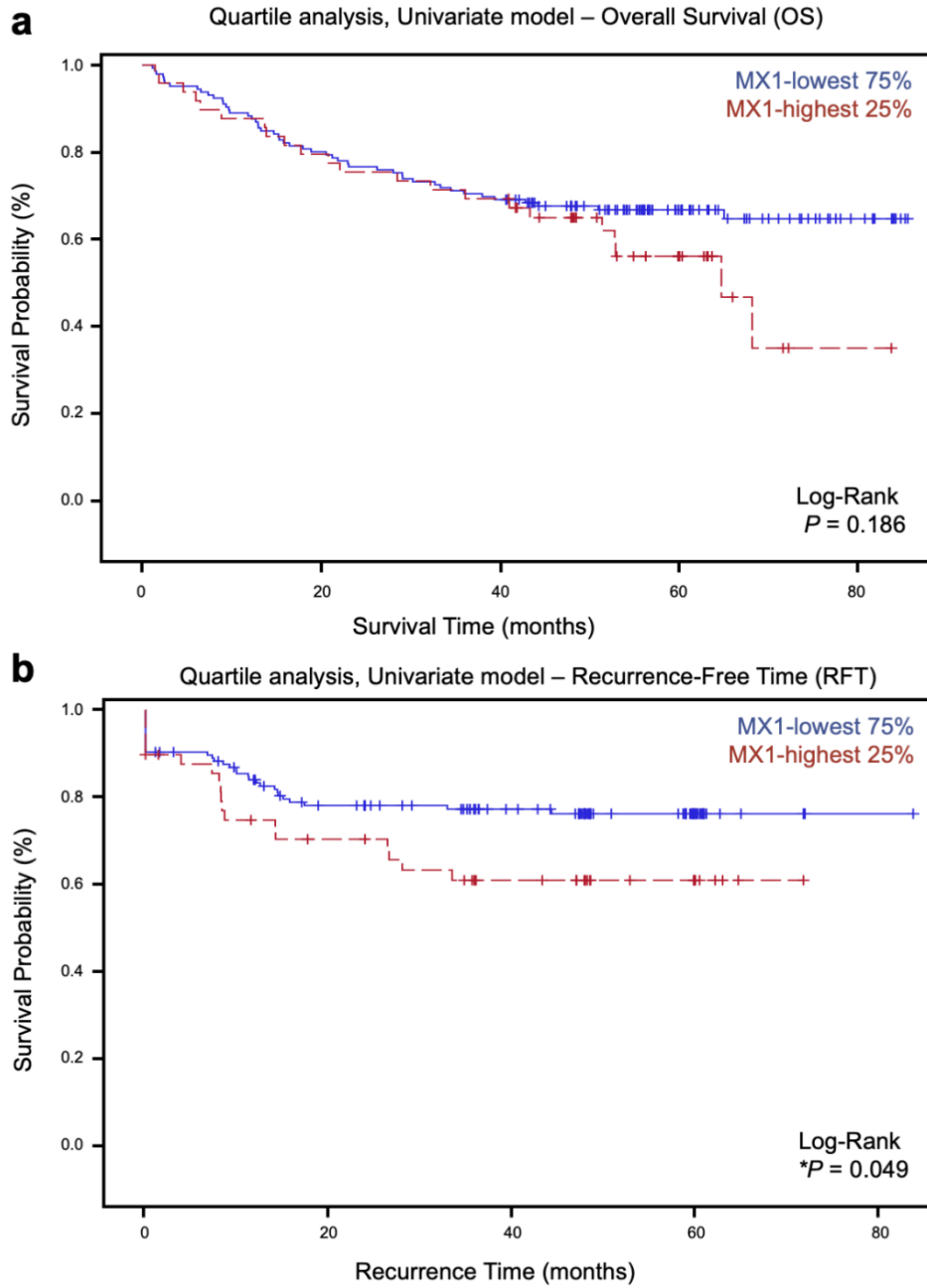ween MX1 and any of these variables, although a non-statistically significant positive association was observed between MX1 score and increased HNSCC cancer stages ($P = 0.09$). Univariate Cox linear regression modeling was used to analyze the association between MX1 score and each variable.

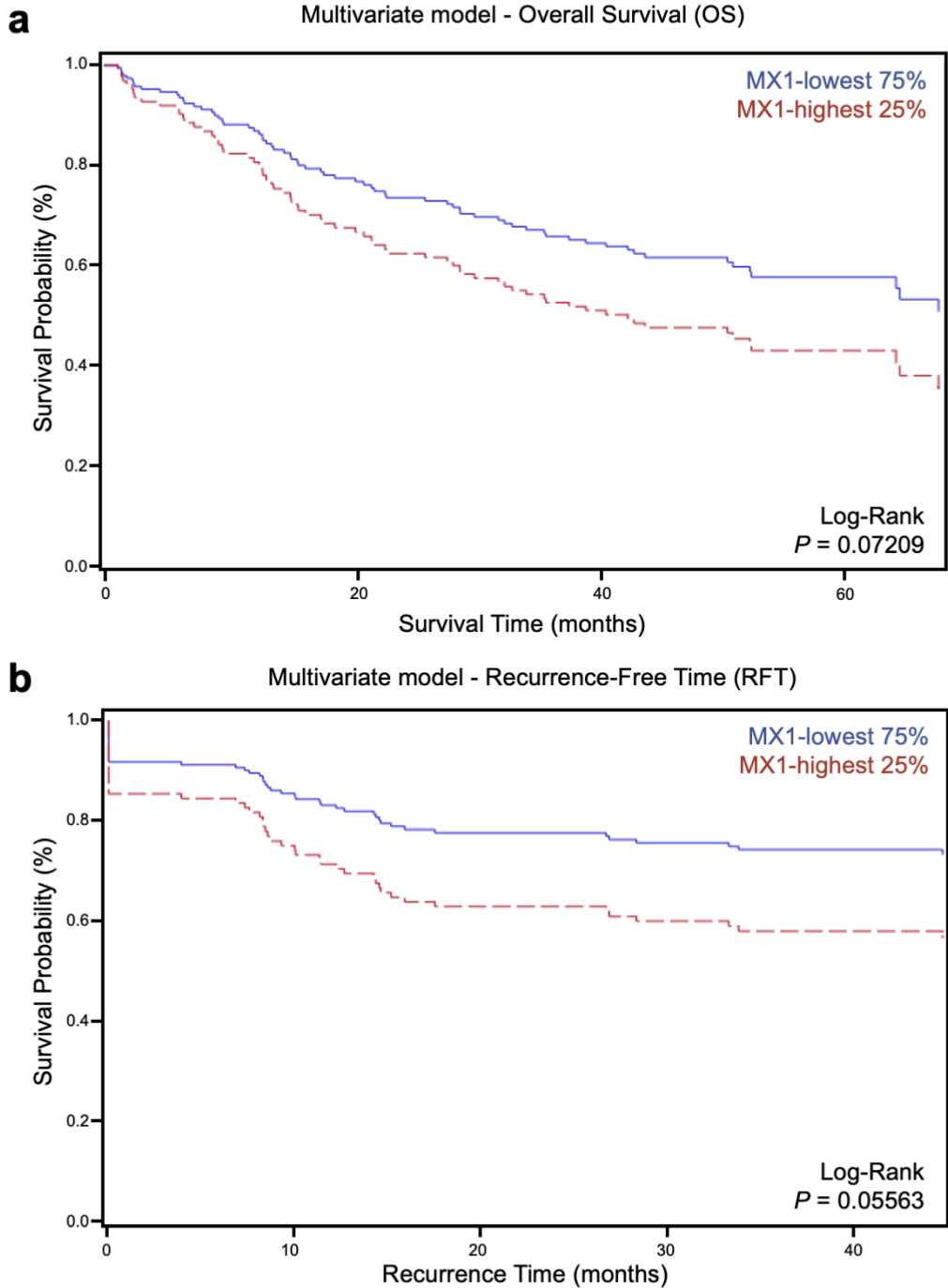**Supplementary Figure 3**

a Quartile analysis, Univariate model – Overall Survival (OS)

b Quartile analysis, Univariate model – Recurrence-Free Time (RFT)

26   **Supplementary Figure 3. a-b** MX1 immunohistochemical scores were segregated for patients

27   in the highest quartile vs. all other patients (lowest 75%) and the Kaplan-Meier curves of each

28   group were compared for overall survival (**a**) or recurrence-free time (**b**) using a log-rank test.

Supplementary Figure 4

a Multivariate model - Overall Survival (OS)

b Multivariate model - Recurrence-Free Time (RFT)
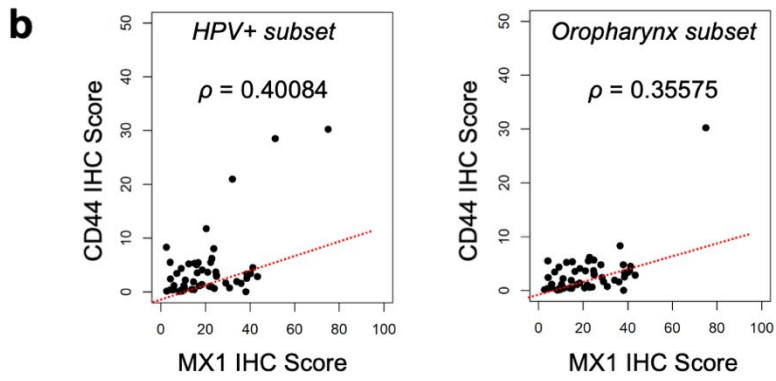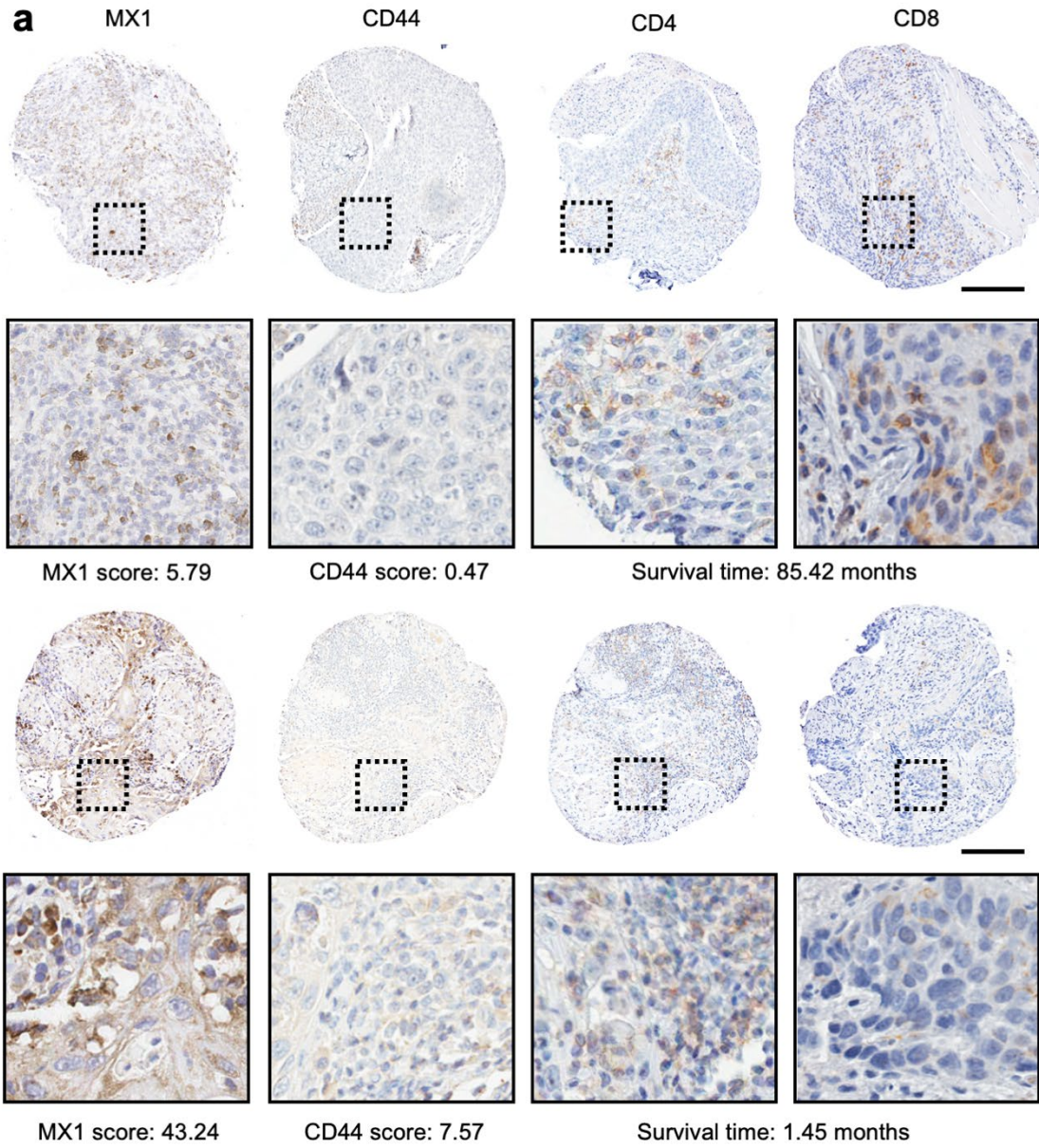
Supplementary Figure 4. a-b MX1 immunohistochemical scores were segregated for patients

in the highest quartile vs. patients in the lowest 75% following construction of a multivariate

34   model which assumes the following parameters: 59 years old, advanced stage (3 or 4), oral

35   cavity cancer, mild comorbidities, and average $CD4^+$ and $CD8^+$ T-cell infiltration (15 cells/mm^2).

36   Kaplan-Meier curves of each group were compared for overall survival (**a**) or recurrence-free

37   time (**b**) using a log-rank test.

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Supplementary Figure 5

a

MX1   CD44   CD4   CD8

MX1 score: 5.79   CD44 score: 0.47   Survival time: 85.42 months

MX1 score: 43.24   CD44 score: 7.57   Survival time: 1.45 months

b

HPV+ subset $\rho = 0.40084$

Oropharynx subset $\rho = 0.35575$

CD44 IHC Score   MX1 IHC Score

41 **Supplementary Figure 5. Representative immunohistochemical staining for MX1 in**

42 **conjunction with CD4, CD8, and CD44.** TMAs were stained for MX1, CD4, CD8, or CD44,

43 followed by quantification of MX1 and CD44 IHC scores selectively within cancer cells. **(a)**

44 Representative images of each marker from an MX1-low core (upper panels**)** or MX1-high core

45 (lower panels). Scale bar: 200 μm. **(b)** The HNSCC cancer stem cell marker CD44 was

46 positively correlated with MX1 in HPV[+] tumors (left panel; n = 54 patients) and oropharyngeal
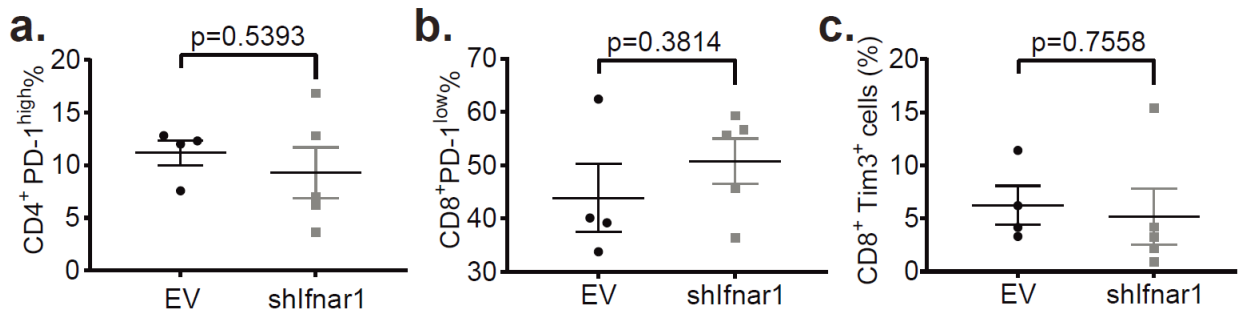
47 tumors (right panel; n = 52 patients).

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Supplementary Figure 6

Supplementary Figure 6. Ifnar1-deficient-tumor bearing mice show comparable effector populations in the spleen. Spleens were harvested 36 days following tumor implantation, and lymphocytes were isolated using a Ficoll-Paque gradient. The proportion of (**a**) CD4$^+$PD-1^{high}, (**b**) CD8$^+$PD-1^{low} and (**c**) CD8$^+$Tim3$^+$ TILs were assessed by flow cytometry. Gating strategy was as follows: Lymphocytes, single cells, Zombie Aqua negative (viability), CD45-positive, CD3-positive (n=4 in the control group and n=5 in the shIfnar1 group). All Comparisons between the two groups were made using a two-tailed unpaired *t* test.

67 **Supplementary Table 1** - Descriptive statistics for MX1 and CD44 immunohistochemical

68 staining scores obtained by Aperio ImageScope quantification of TMAs. MX1 scores were

69 available from 195 patients, CD44 scores were available from 262 patients, and both MX1 and

70 CD44 scores were available from 181 HNSCC patients.

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Protein	n	Mean	SD	Median	Minimum	Maximum	25th Percentile	75th Percentile
MX1	195	22.01	16.925	18.534	0.1144	86.25	9.33	31.94
CD44	262	7.39	8.128	4.577	0.0375	40.68	1.475	10.31

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74 **Supplementary Table 2.** Number of cells detected for each tumor immune cell cluster identified

75 by single cell RNA-sequencing and immune cell deconvolution.

Cell cluster	Cell identity	Total number of cells detected
Cluster 1	Myeloid-derived suppressor cells	2112
Cluster 2	Myeloid-derived suppressor cells	1263
Cluster 3	Tcf7$^+$ CD4$^+$ T-cells	1217
Cluster 4	CXCR5$^+$ B-cells	1066
Cluster 5	Myeloid-derived suppressor cells	1009
Cluster 6	Tbet1$^+$ PD1$^+$ CD8$^+$ T-cells	906
Cluster 7	Myeloid-derived suppressor cells	778
Cluster 8	Myeloid-derived suppressor cells	684
Cluster 9	Myeloid-derived suppressor cells	674
Cluster 10	CXCR5$^+$ B-cells	598
Cluster 11	CXCR5$^+$ B-cells	507
Cluster 12	Myeloid-derived suppressor cells	500
Cluster 13	M2-like macrophages	471
Cluster 14	Tumor cells	292
Cluster 15	Regulatory T-cells	220
Cluster 16	$\gamma\delta$ T-cells	219
Cluster 17	Natural killer cells	174
Cluster 18	Tcf7$^+$ CD8$^+$ T-cells	143
Cluster 19	Basophils	47
Cluster 20	Conventional dendritic cells type 1	27

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