MAIT Cell Abundance Within Solid Tumors Is Associated with Key Clinical Characteristics

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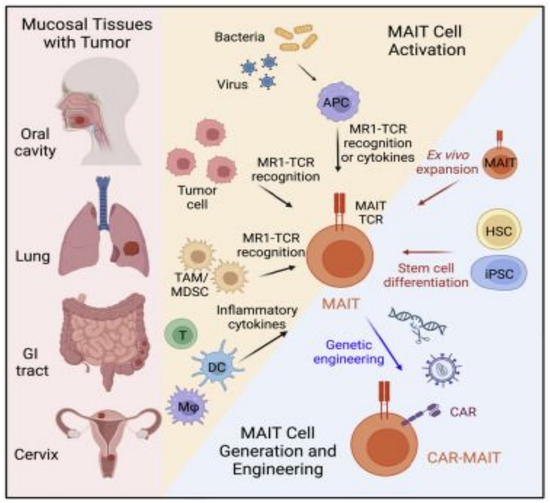
Poster/Abstract #

INTRODUCTION

- Mucosal-associated invariant T (MAIT) cells are an innate-like T cell subset, defined by semi-invariant TCRα chains that recognize microbial-derived vitamin B metabolites presented by the non-polymorphic MR1 molecule.
- The TCRα chains expressed by MAIT cells predominantly utilize TRAV1-2-TRAJ33/20/12 [1].
- Upon activation, they produce IFN-γ, TNF-α, IL-17, and cytotoxic molecules such as granzyme B and perforin.
- In cancer, MAIT cells exhibit both anti- and pro-tumor functions, with their frequency and activation status in blood or tumors correlating with prognosis in colorectal, hepatocellular, and lung cancers.
- The current study used intratumoral TCR-seq on real-world data to examine the relationship between MAIT cell prevalence, cancer development and therapy response across multiple tumor types.

METHODS

- The Tempus de-identified real-world, multi-modal database was analyzed for solid tumors with TCR sequencing data (N=190,189), defining MAIT-associated TCRα chains by TRAV1-2 and TRAJ33 presence or clonotypes from Loh et al. [1].
- MAIT cell abundance was determined by the total number of clonotypes mapped to MAIT TCRα chains. In multivariate models, total TCRα counts adjusted for overall T cell infiltration.
- Univariate testing assessed MAIT cell prevalence across clinical and demographic variables, including age, race, sex, microsatellite instability (MSI), and PD-L1 status.
- Additionally, multivariate linear models were utilized, adjusting for covariates and total detected TCRα abundance. RNA-seq from matched samples was used to correlate MAIT cell abundance with T cell markers such as GZMB and MR1. MAIT cell abundance was tested across each indication for prognostic association, along with co-occurrence of bacterial and viral strains, including HPV and EBV, detected through next-generation sequencing.



SUMMARY

- Mucosal-associated invariant T (MAIT) cells represent a unique set of T cells bridging the innate and adaptive immune systems. MAIT cells can directly respond to bacterial and fungal pathogens, but can also drive inflammatory and cytotoxic responses through cytokine-mediated mechanisms.
- In the context of cancer, MAIT cells can mediate both pro- and anti-tumorigenic effects[1]. Owing to their MHC-independent mechanism of action, MAIT cells represent a promising avenue for cell therapy, as they may minimize potential off-target toxicities.
- Understanding the prognostic and predictive role of MAIT cells in response to different therapies could help in the identification of potential populations that may benefit from therapies employing MAIT cells. Further integration of MAIT cells and co-occurrence with other immune subtypes and tumor-associated bacteria could identify novel insights into the tumor microenvironment.

RESULTS

Figure 1 & 2. Presence of MAIT Cells Are Associated with Age and Smoking Status (Pan-Cancer)

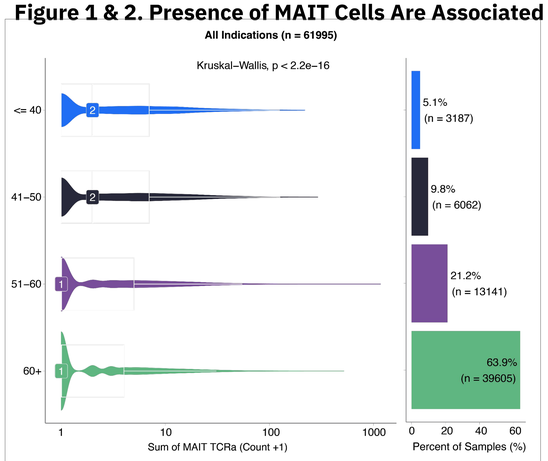


Figure 1. MAIT Cell Abundance by Age

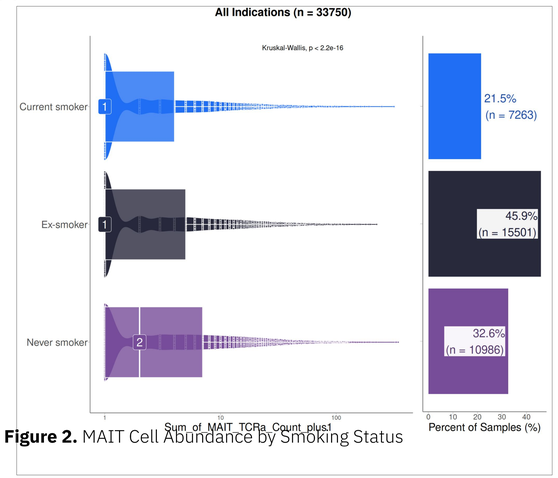


Figure 2. MAIT Cell Abundance by Smoking Status

Figure 3. Age Group and Smoking, MSI, and PD-L1 status all significantly associated with presence of MAIT cells (Pan-Cancer)

Forest Plot of GLM Coefficients for All Indications

Variable		N	Estimate	p
Sex	Female	9432	Reference	
	Male	8487	0.09 (0.08, 0.11)	<0.001
Race	Asian	590	Reference	
	Black or African American	2026	−0.13 (−0.18, −0.09)	<0.001
	Other Race	1044	−0.06 (−0.11, −0.02)	0.007
	White	14259	−0.08 (−0.11, −0.04)	<0.001
Ethnicity	Hispanic or Latino	1223	Reference	
	Not Hispanic or Latino	16696	0.03 (0.00, 0.06)	0.024
Age Group	<= 40	814	Reference	
	41–50	1731	0.01 (−0.02, 0.05)	0.460
	51–60	3775	−0.08 (−0.11, −0.04)	<0.001
	60+	11599	−0.12 (−0.15, −0.09)	<0.001
Smoking Status	Current smoker	3430	Reference	
	Ex−smoker	7706	0.05 (0.03, 0.06)	<0.001
	Never smoker	6783	0.11 (0.09, 0.13)	<0.001
Overall Stage 4	Stage 4	13497	Reference	
	Stage Other	4422	−0.05 (−0.06, −0.03)	<0.001
HPV+ Status	Negative	22	Reference	
	Not Available	17826	0.03 (−0.16, 0.22)	0.747
	Positive	71	0.12 (−0.10, 0.33)	0.281
MSI Status	high	539	Reference	
	stable	17380	0.11 (0.07, 0.15)	<0.001
PD-L1 (TPS)	1% <= TPS < 49%	5061	Reference	
	TPS < 1%	11080	0.09 (0.08, 0.11)	<0.001
	TPS >= 50%	1778	−0.09 (−0.11, −0.06)	<0.001
Sum of MAIT TCRa log10 (Count +1)		17919	0.28 (0.27, 0.29)	<0.001

Figure 4A & B. Presence of MAIT Cells Are Associated with MSI Stable in Patients with CRC

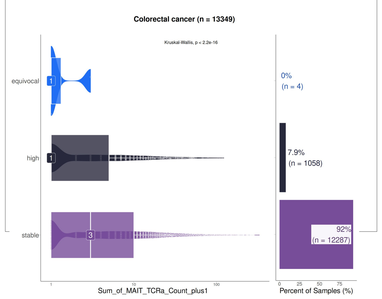


Figure 4A . MAIT cell Abundance by MSI status

Forest Plot of GLM Coefficients for Colorectal cancer - Sum_of_MAIT_TCRa_Count_log10

Variable		N	Estimate	p
sex	Female	1221	Reference	
	Male	1674	0.11 (0.07, 0.14)	<0.001
race	Asian	112	Reference	
	Black or African American	348	−0.15 (−0.25, −0.04)	0.006
	Other Race	215	−0.01 (−0.13, 0.11)	0.875
	White	2220	−0.03 (−0.12, 0.06)	0.524
ethnicity	Hispanic or Latino	260	Reference	
	Not Hispanic or Latino	2635	0.05 (−0.01, 0.12)	0.113
age_group	≤ 40	207	Reference	
	41-50	474	−0.08 (−0.16, 0.00)	0.054
	51-60	719	−0.14 (−0.21, −0.06)	<0.001
	60+	1495	−0.19 (−0.26, −0.12)	<0.001
smoking_status	Current smoker	391	Reference	
	Ex-smoker	988	0.03 (−0.03, 0.09)	0.314
	Never smoker	1516	0.03 (−0.02, 0.09)	0.230
overall_stage_4	Stage 4	2276	Reference	
	Stage Other	619	−0.07 (−0.12, −0.03)	0.002
msi_status	high	211	Reference	
	stable	2684	0.20 (0.13, 0.27)	<0.001
PDL1_IHC_TPS	1% ≤ TPS < 49%	303	Reference	
	TPS < 1%	2567	0.13 (0.07, 0.19)	<0.001
	TPS ≥ 50%	25	−0.08 (−0.28, 0.12)	0.421
Sum_of_TCRa_Count_log10		2895	0.41 (0.38, 0.45)	<0.001

Figure 4B . Multivariable Forest Plot of Key Cancer Characteristics on MAIT cell presence in CRC patients.

Figure 5. MAIT Cell Abundance is lower in PD-L1 High Patients in NSCLC

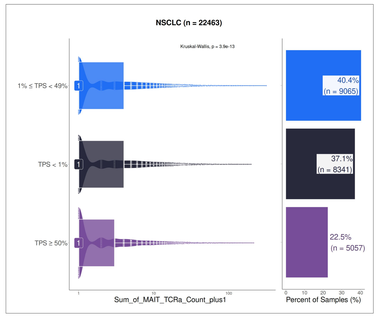


Figure 5A. MAIT Cell Abundance by PD-L1 Status. Trend is consistent pan-cancer

Forest Plot of GLM Coefficients for NSCLC - Sum_of_MAIT_TCRa_Count_log10

Variable		N	Estimate	p
sex	Female	2674	Reference	
	Male	2926	0.03 (0.01, 0.05)	0.012
race	Asian	183	Reference	
	Black or African American	595	−0.15 (−0.22, −0.08)	<0.001
	Other Race	222	−0.05 (−0.13, 0.03)	0.219
	White	4600	−0.11 (−0.17, −0.05)	<0.001
ethnicity	Hispanic or Latino	226	Reference	
	Not Hispanic or Latino	5374	0.04 (−0.02, 0.09)	0.217
age_group	≤ 40	43	Reference	
	41-50	234	−0.03 (−0.17, 0.10)	0.606
	51-60	961	−0.16 (−0.29, −0.04)	0.010
	60+	4362	−0.17 (−0.29, −0.05)	0.007
smoking_status	Current smoker	1651	Reference	
	Ex-smoker	3240	0.05 (0.03, 0.08)	<0.001
	Never smoker	709	0.15 (0.11, 0.19)	<0.001
overall_stage_4	Stage 4	3657	Reference	
	Stage Other	1943	−0.01 (−0.03, 0.01)	0.467
msi_status	high	33	Reference	
	stable	5567	0.17 (0.03, 0.31)	0.018
PDL1_IHC_TPS	1% ≤ TPS < 49%	2188	Reference	
	TPS < 1%	2130	0.01 (-0.01, 0.04)	0.301
	TPS ≥ 50%	1282	-0.09 (-0.12, -0.06)	<0.001
Sum_of_TCRa_Count_log10		5600	0.25 (0.23, 0.27)	<0.001

Figure 5B . Multivariable Forest Plot of Key Cancer Characteristics on MAIT cell presence in NSCLC patients.

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