Clinicopathological correlation of PD-L1 and CD8 expression in a series of 100 DNA mismatch repair protein proficient (pMMR) and deficient (dMMR) colorectal cancers

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Background and Aims

Colorectal carcinoma (CRC) is a major global health concern, ranking as the third most diagnosed cancer worldwide. It is a heterogeneous disease, with the deficient mismatch repair (dMMR) subtype exhibiting distinct immune responses and favorable outcomes with immunotherapy. Programmed death-ligand 1 (PD-L1) expression plays a critical role in immune evasion by tumors. This study aims to explore PD-L1 expression in both dMMR and proficient mismatch repair (pMMR) Colorectal carcinoma to elucidate potential therapeutic targets and the underlying mechanisms driving its expression.

Methodology

This retrospective study analyzed 100 colorectal carcinoma (CRC) cases, comprising 53MMR-deficient and 47 MMR-proficient cases. Immunohistochemistry (IHC) was used to stain for PD-L1 and CD8 T-cells, and PCR for microsatellite instability (MSI) validated the MMR-deficient phenotype. PD-L1 expression was scored in tumour and immune cells using a Combined Positive Score (CPS: 0, ≥ 1, or ≥ 10). Digital image analysis quantified CD8 populations, and results were correlated with clinical and pathological variables to assess the association of PD-L1 with these features.

Results

- There was 100% concordance between MMR (IHC) and MSI (PCR).
- PD-L1 positivity rate in MMR-deficient tumors was 41.51%, higher than in MMR-proficient tumors (23.40%).
- Positive correlation between CD8 and PD-L1 expression levels, suggesting potential co-regulation between CD8+ T-cells and PD-L1 with tumor stage in MMR-deficient.
- A subgroup (23%) of pMMR had high PD-L1 expression suggesting a potential role for immune-checkpoint inhibitors in this subgroup.

Correlations

			Tumor Stage	CD8 expression (cell count mm2)	PD-L1 expression CPS Score <10 for negative and >=10 for positive	PDL1 expression subgroup (<1, >1 & <10, >=10)
Spearman's rho	Tumor Stage	Correlation Coefficient	1	-.350*	-.391**	-.301*
		Sig (2-tailed)	.	0.01	0.004	0.028
		No of cases	53	53	53	53
	CD8 expression (cell count mm2)	Correlation Coefficient	-.350*	1	.548**	.470**
		Sig (2-tailed)	0.01	.	<.001	<.001
		No of cases	53	53	53	53
	PD-L1 expression CPS Score <10 for negative and >=10 for positive	Correlation Coefficient	-.391**	.548**	1	.915**
		Sig (2-tailed)	0.004	<.001	.	<.001
		No of cases	53	53	53	53
	PDL1 expression subgroup (<1, >1 & <10, >=10)	Correlation Coefficient	-.301*	.470**	.915**	1
		Sig (2-tailed)	0.028	<.001	<.001	.
		No of cases	53	53	53	53

*. Correlation is significant at the 0.05 level (2-tailed). **. Correlation is significant at the 0.01 level (2-tailed).

Table 1: Correlation between tumor stage, CD8 expression and PD-L1 expression in dMMR.

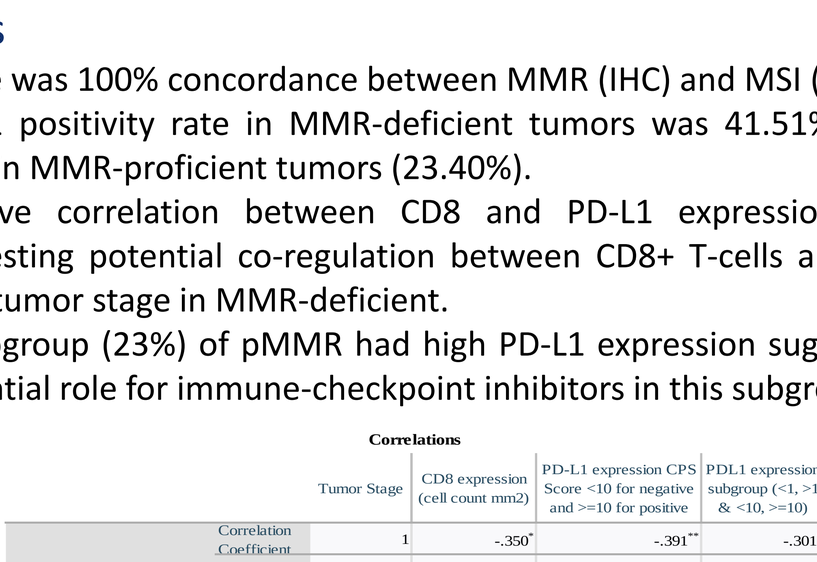

Figure 1: *CD8 expression vs PD-L1 expression CPS Score in dMMR*

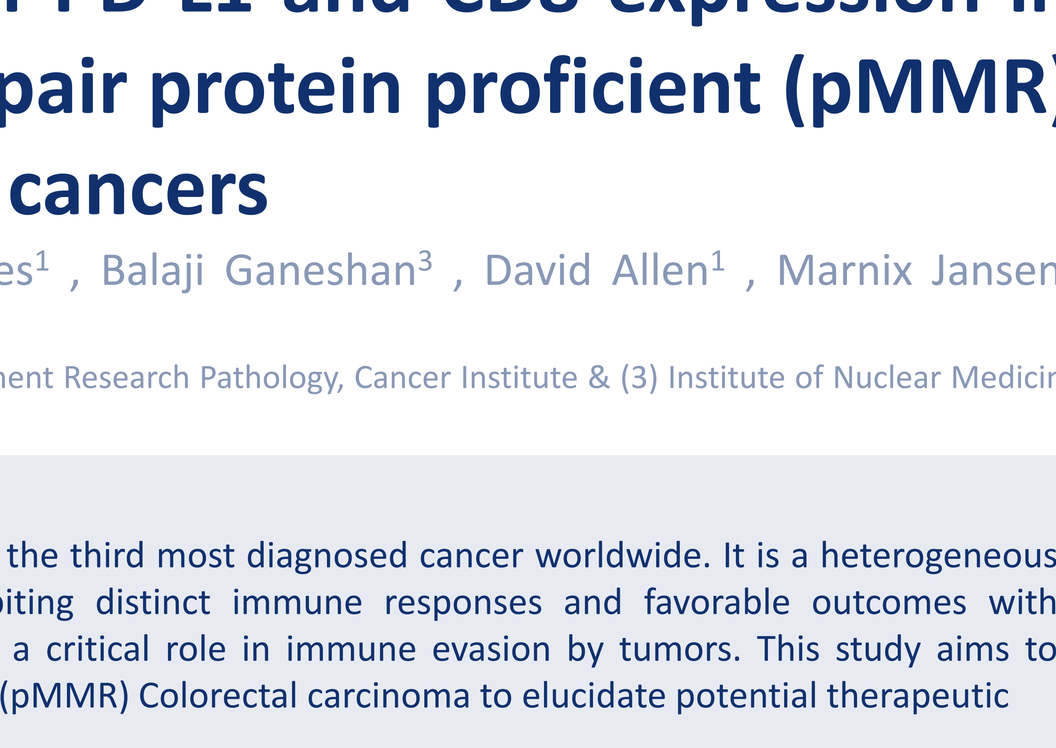

Figure 2: *Positive correlation between PD-L1 expression and CD8 T-cells in dMMR*

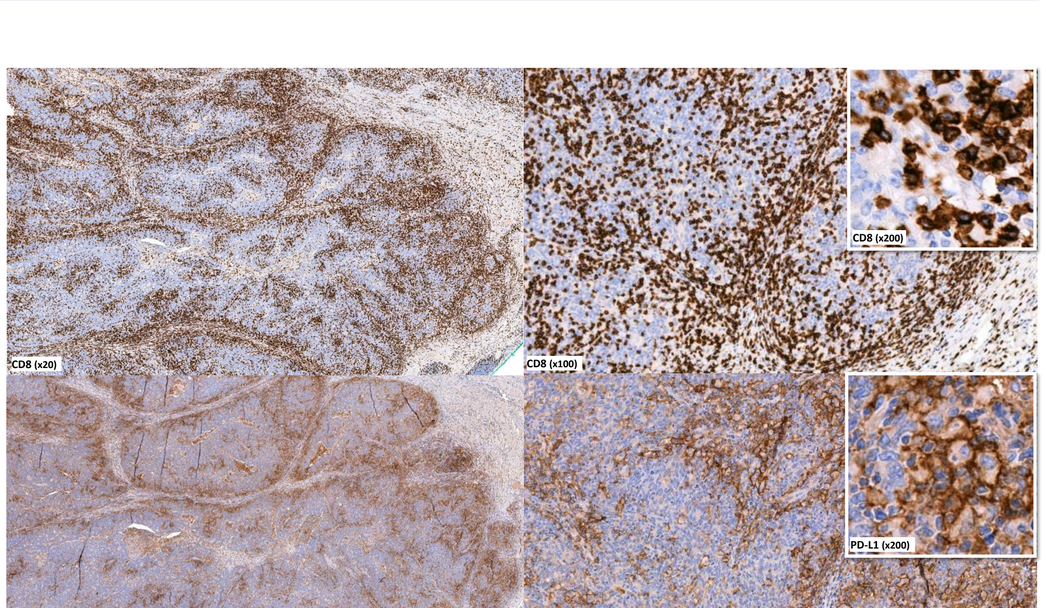

Figure 3: *Low PD-L1 expression and High CD8 T-cells in pMMR*

Conclusion

This study demonstrates a higher prevalence of PD-L1 expression in MMR-deficient colorectal carcinoma (CRC), suggesting a potential immunogenic phenotype, particularly given the high CD8 expression observed. The association with advanced TNM stages emphasizes the importance of PD-L1 in tumor progression, providing insights into its heterogeneous expression and potential as a therapeutic target in MMR-deficient CRC. Additionally, a subset of MMR-proficient CRC cases (11 out of 47) exhibited high PD-L1 expression, indicating that a specific subgroup of pMMR CRC may benefit from immune checkpoint inhibitors.

References

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