Immunologic biomarkers in a multi-center, single arm, open label Phase II clinical trial of mFOLFOX6 and pembrolizumab in patients with advanced colorectal cancer

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Disclosures

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- Study funded in part by a grant from Merck & Company, Inc.
- I have no conflicts of interest to disclose
- I am not discussing the off-label or unapproved use of drugs outside of a clinical trial setting

Checkpoint blockade in CRC: limited success to date

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- PD-1 checkpoint blockade has been of limited effectiveness in CRC
- One subset (MSI^{Hi}) have responded quite well, while MSS patients have not
- Theorized to be due to relative lack of neo-antigens in MSS
- NCT02375672: Patients with advanced colorectal cancer treated with Pembrolizumab + mFOLFOX6
- Hypothesis: Chemotherapy may potentiate the clinical response to pembrolizumab and improve outcomes in CRC, while modulating immunologic biomarkers important in treatment efficacy

Of 30 patients:			
RECIST:	1 CR	irRC:	0 IRCR
	7 PR		16 IRPR
	8 SD		9 IRSD
	14 PD		5 IRPD

Median PFS: 11.3 mo.
Median OS: Not reached (76% of patients alive, median follow up of 17.7 mo.)

Baseline immune phenotype and association with patient outcome?

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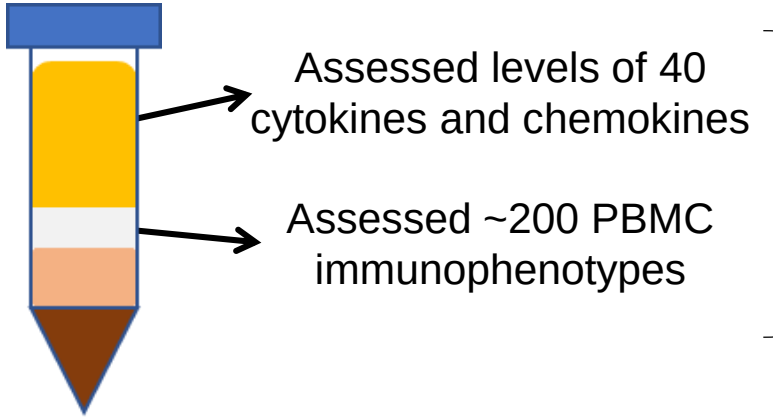
Experimental Approach

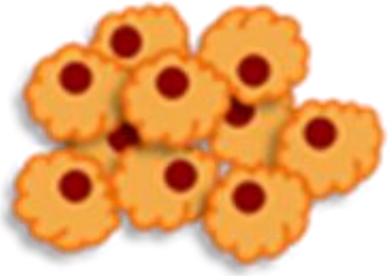
Obtain blood from patients at baseline, Cycle 1 Day 15, and Cycle 3 Day 1



- Relationship to PFS
- Relationship to OS
- Relationship to Clinical Response

Archival tumor samples (FFPE) obtained from 14/30 patients

- Analysis ongoing



Expression of T-cell checkpoint molecules associated with response to pembro + FOLFOX

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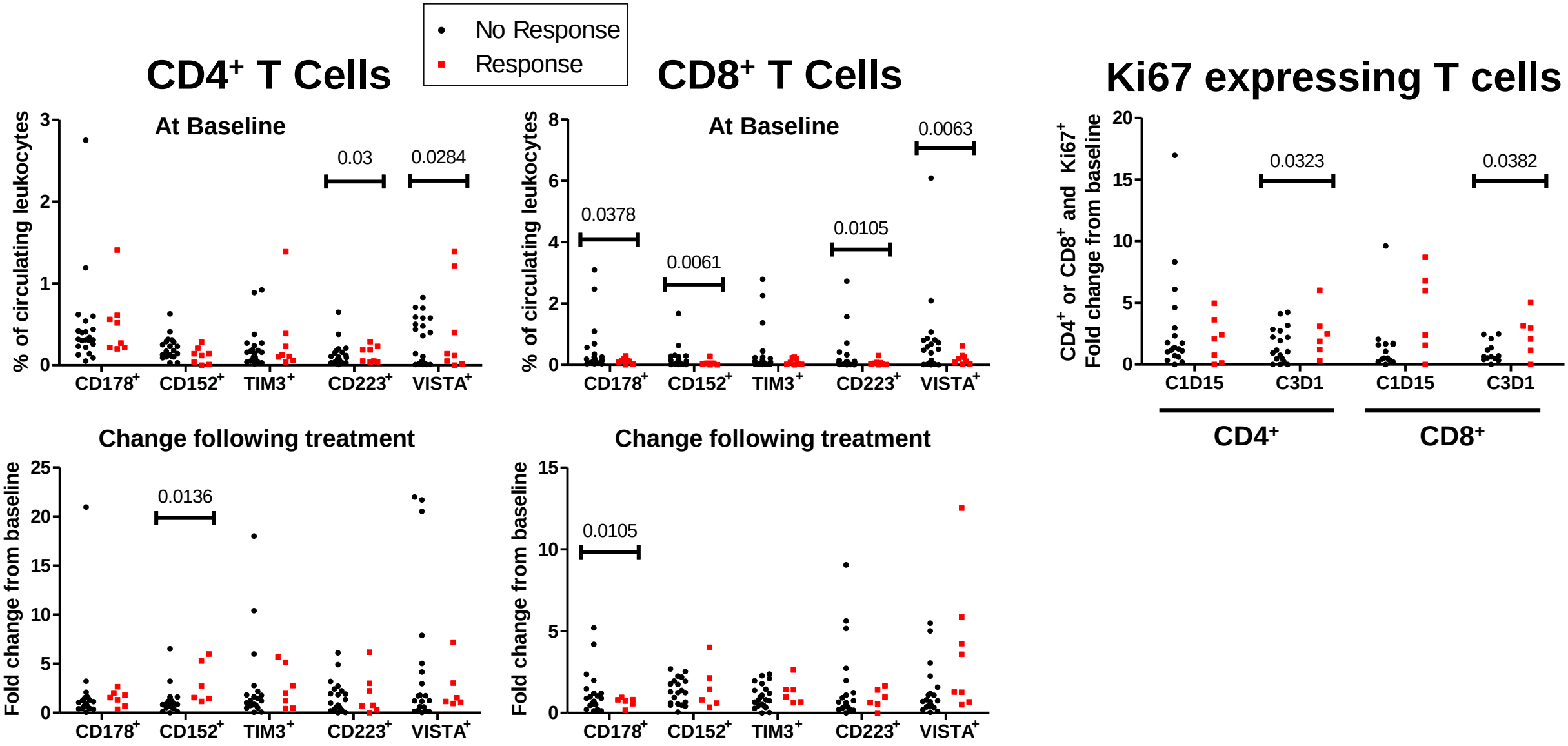

Expression of cytokines and chemokines associated with response to pembro + FOLFOX

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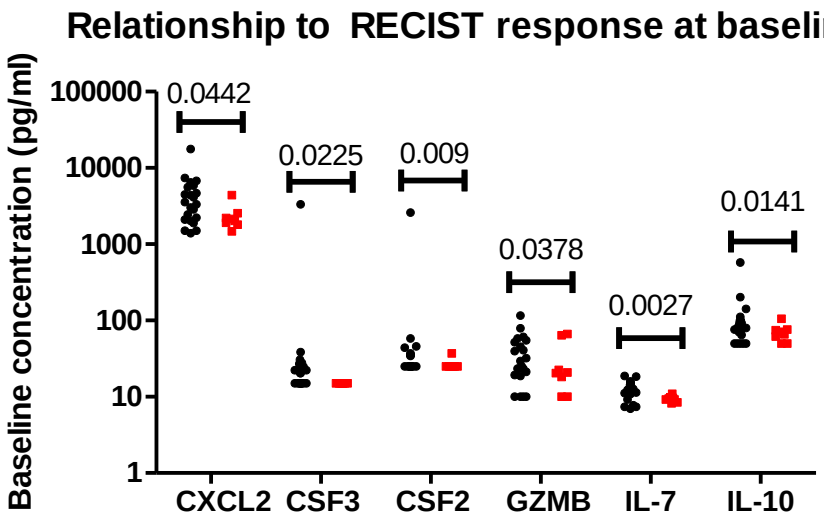
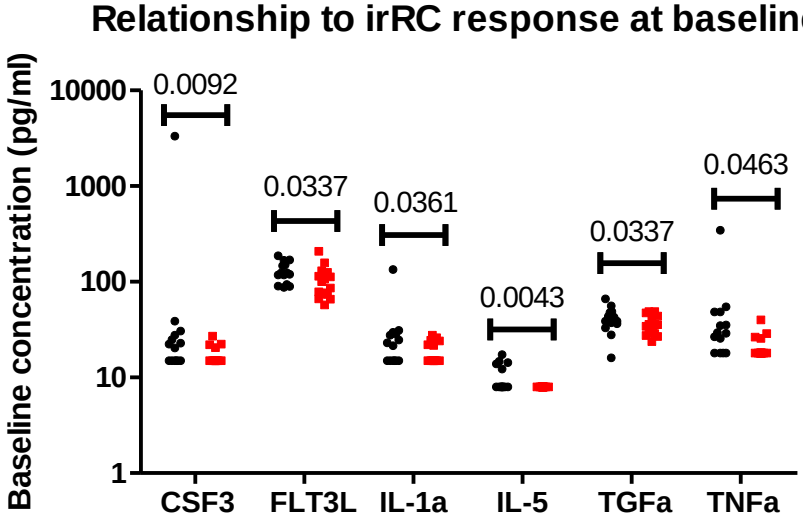
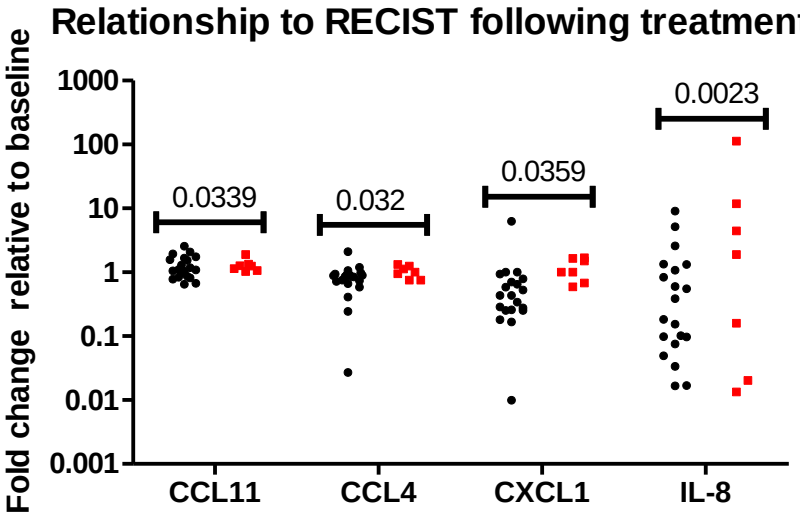
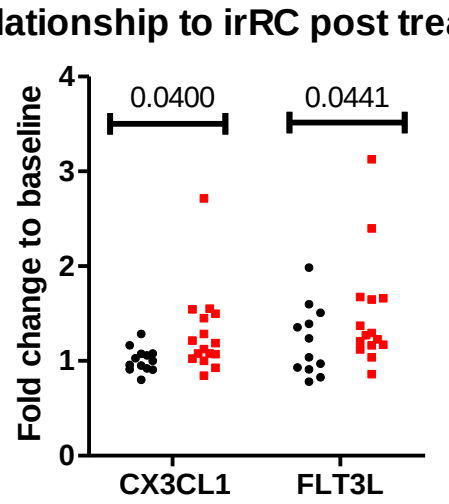
- No Response
- Response









Conclusions

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- Baseline levels of several circulating (systemic) soluble factors were independently associated with beneficial response to combination pembrolizumab + FOLFOX. (e.g. G-CSF)
- Changes in the level of several circulating soluble factors were independently associated with clinical response (CR, PR) to pembrolizumab + FOLFOX. (e.g. IL-8)
- Relative expression of T-cell checkpoint molecules on circulating $CD4^+$ and $CD8^+$ T cells prior to treatment was strongly and independently associated with clinical response to pembrolizumab + FOLFOX. (e.g. LAG3)
- Changes in the expression of T-cell checkpoint molecules on circulating $CD4^+$ and $CD8^+$ T cells following treatment was predictive of clinical response to treatment. (e.g. CTLA4)
- Please visit poster P290 for a more in-depth discussion of this research.

Acknowledgements

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