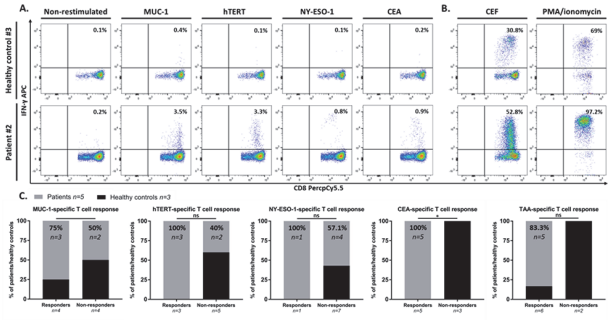
one healthy control (figure 1). When TAA responses were pooled together, 83.3% of responders were patients (n=5) and 100% of non-responders were healthy controls (n=2).



Abstract 758 Figure 1 CRC TAA-specific CD8 T cell responses in CRC patie

Dot plot of one representative healthy control (#3) and one representative patient (#2) showing IFN-γ production by CD8 T cells in response to (A) MUC-1, hTERT, NY-ESO-1 and CEA stimulations or without any restimulation (negative control) and (B) positive controls (CEF and PMA/ionomycin). Percentages of IFN-gamma+ CD8 T cells are displayed in each plot. C Frequency of MUC-1-, hTERT-, NY-ESO-1-, CEA- and pooled TAA-specific CD8 T cell responses in patients (grey) and healthy controls (black). Fisher exact test, * p=0.0179; ns=not significant.

Conclusions The presence of circulating T cells responding to CEA in all 5 patients, but also to MUC-1 and hTERT in 3 patients suggests that these TAAs may be good targets for immunotherapy in CRC. Our findings also provide a rationale to investigate the prognostic value of CEA-, MUC-1- and hTERT-specific T cells in the peripheral blood of CRC patients and to consider vaccination with these antigens to boost or induce responses to control residual tumor post-surgery.

Ethics Approval This study was approved by Health Sciences North's Research Ethics Board; approval number 18- 104.

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759 DEVELOPMENT OF AN IMPLANTABLE ARTIFICIAL LYMPH NODE AS A THERAPEUTIC CANCER VACCINE

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Background Personalized therapeutic cancer vaccines aim to target and reprogram the host immune system to achieve cancer eradication in situ. Cancer vaccines deliver two main components: immunostimulants (iS) and tumor antigens to reduce tumor burden with a robust T cell response; however, none have reached broad clinical success due to difficulty in vaccine administration, ex vivo cellular manipulation, low clinical efficacy and broad administrative barriers. While most efforts to date have focused on repeated bolus administrations, biomaterial-based vaccine strategies have led to promising clinical translation.

Methods In light of these challenges, we have designed a clinically-viable platform-based vaccine strategy, termed the NanoLymph, to provide spatiotemporal elution of immunostimulants and tumor antigens locally to recruit and activate antitumor immunity for cancer eradication. Here, we aim to target the release of granulocyte macrophage colony stimulating factor (GM-CSF) and TLR-7/8 agonist Resiquimod (R848) to promote recruitment and activation of dendritic cells (DCs), a key player in antitumor cytotoxicity.

Results We demonstrate the NanoLymph as an structurally stable and biocompatible immunostimulatory niche for durable DC-driven tumor specific T-cell mediated cytotoxicity. Additionally, we demonstrate the NanoLymph's ability to recruit and activate immune cells of interest, activating antitumor immunity against model antigen. Thus, we have provided the framework necessary to develop a personalized therapeutic cancer vaccine for tumor-specific T-cell mediated responses necessary to generate immunological memory.

Conclusions Future studies will evaluate immunostimulant and tumor antigen biodistribution in vivo and further apply the NanoLymph in a tumor bearing model to effect antitumor cytotoxicity. Ultimately, we aim to develop a personalized platform applicable for every patient of any cancer type aimed at direct clinical translation.

Ethics Approval This study was approved by the Houston Methodist Research Institute (HMRI), according to protocols approved by the Institutional Animal Care and Use Committee (IACUC). HMRI's Animal Welfare Assurance number is A4555-01. HMRI assures strict compliance with all federal regulations and guidelines involving the use of laboratory animals in biomedical research.

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760 TROUGH LEVELS OF IPILIMUMAB IN SERUM AS A POTENTIAL PREDICTIVE BIOMARKER OF CLINICAL OUTCOMES FOR PATIENTS WITH ADVANCED MELANOMA AFTER TREATMENT WITH IPILIMUMAB

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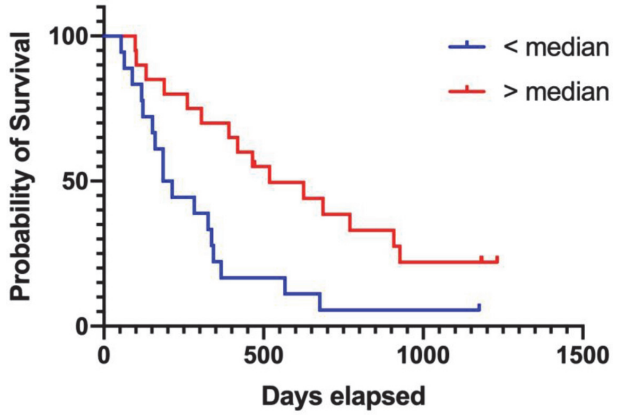
Background Immune checkpoint blockade (ICB) using anti-CTLA-4 and anti-PD-1/PD-L1 has revolutionized the treatment of advanced cancer. However, ICB cures only a fraction of patients, and biomarkers such as PD-L1 expression or CXCL11 have suboptimal sensitivity and specificity. Exposure-response (E-R) relationships have been observed in other therapeutic mAbs. There are many factors that can influence E-R,[1] yet several studies have shown that trough levels of anti-PD-1/PD-L1 correlated with clinical outcomes. Little is known about the potential utility of anti-CTLA-4 levels as a predictive biomarker.

Methods Serum was obtained after doses 2 and 4 from patients with advanced melanoma who received ipilimumab alone (3 mg/kg every 3 weeks for 4 treatments) via an expanded access program. We have successfully established a proteomics assay to measure ipilimumab concentration in serum using a versatile LC-MS/MS-based nano-surface and molecular-orientation limited proteolysis (nSMOL) approach.[2]

Results Serum samples from 38 patients were assessed for the ipilimumab trough levels by the nSMOL assay. The ipilimumab concentrations after dose 2 were ranged between 4.44 and 33.63 ug/ml (median:16.30, IQR: 11.41 – 20.87). We found that patients with lower serum trough levels of

ipilimumab had poorer overall survival when we grouped patients based on the ipilimumab trough level (figure1 Median survival: < median = 199.5 days, > median = 519.0 days. Log-rank test: p = 0.0057). A similar result was observed for ipilimumab trough levels after dose 4. We also found that trough levels of ipilimumab inversely associated with CXCL11 (p = 0.0095. R^2 = 0.1818), a predictive biomarker we previously identified,[3] and soluble CD25 (sCD25) (p = 0.0038. R^2 =0.2210), a prognostic biomarker for advanced melanoma but not with other biomarkers such as absolute lymphocyte counts, LDH, VEGF, sMICA, and sMICB.



Abstract 760 Figure 1 Poorer OS in patients with lower trough levels of ipilimumab
Patients with lower serum trough levels of ipilimumab had poorer overall survival when we grouped patients based on the ipilimumab trough level (Median survival: < median = 199.5 days, > median = 519.0 days. Log-rank test: p = 0.0057).

Conclusions Our results suggest that the trough levels of ipilimumab might be a useful predictive biomarker for the long-term survival of the patients with advanced melanoma treated by ipilimumab. The weak association of ipilimumab trough levels with CXCL11 and sCD25 as well as no association with known biomarkers highlights the potential usefulness of trough levels of ipilimumab as the biomarker. Further studies are required to understand the mechanisms for lower levels of ipilimumab in refractory patients to improve the efficacy of ICB.

Acknowledgements This study was funded by Providence Portland Medical Foundation and Shimadzu Corporation.

Trial Registration NCT00495066

Ethics Approval All patients provided written informed consent and all studies were carried out in accordance with the Declaration of Helsinki under good clinical practice and Institutional Review Board approval.

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POTENTIAL PREDICTIVE BIOMARKERS OF RAPID PROGRESSION AND RESPONSE TO ANTI-PD1 TREATMENT BY GENE PROFILING ANALYSIS IN METASTATIC MELANOMA PATIENTS

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Background Immunotherapy dramatically changed the landscape of melanoma treatment. Even if nearly 40% of patients has a long-term benefit from anti-PD-1 agents, nearly 30% relapse in the first year of treatment, showing in some cases very rapid disease progression. Actually, there are no effective biomarkers that could predict patient's clinical benefit. Aim of this study is to identify gene profiling biomarkers that could help to select melanoma patients who most likely respond to anti-PD-1 therapy.

Methods We defined as fast responder (FR) or fast progressor (FP) patients who got clinical response or clinical progression within eight weeks from first cycle of therapy. We retrospectively collected data from 51 metastatic melanoma patients (25 FR and 26 FP) treated from October 2016 to June 2020 in first-line with anti-PD1 monotherapy (nivolumab or pembrolizumab) at National Cancer Institute of Naples, Italy. Gene expression profiling analysis was performed using NanoString® IO 360 panels on PBMCs collected at baseline from 18 patients (10 FR and 8 FP). Patients with ECOG≥2 were excluded. They were all IV stage (5 M1a, 1 M1b, 12 M1c) of which 15 were B-RAF wild-type (83%) and 3 were B-RAF mutated (17%). Statistical associations between treatment response and gene score variables were estimated through Bonferroni correction for multiple comparisons and Benjamini-Hochberg.

Results Patterns of gene expression were assessed for correlation to response. We compared PBMCs Nanostring analysis between FR and FP patients. We found a higher expression of KRas, CD39, IFI16, IL18, FCGR2A, IL1RN, MAP3K8, TLR5, TLR8, MyD88 and NF-kB in FP patients (all with p-value ≤0.005), most of them related to cell proliferation and immunosuppressive mechanism. Instead we found a higher expression of PRF1, PIK3R1, HLA-DPA1, HLA-DRB1, HLA-DOA, CD45RA, LDHB, KIR3DL2, CD2, CD28, CD7, CD27 in FR patients (all with p-value ≤0.01), most of them related to priming and cytolysis.

Conclusions Our study suggests that a specific gene signature may discriminate FR or FP patients. These preliminary data provide a rationale for further investigating gene profiling signature as a potential biomarker of response to immunotherapy.

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Ethics Approval The study was approved by the internal ethics board of the Istituto Nazionale Tumori IRCCS Fondazione 'G. Pascale' of Napoli Italy, approval number of registry 17/17 OSS.

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