Assessment of Tumor Infiltrating Lymphocyte therapy for metastatic epithelial cancers using Patient Derived Tumor Organoids

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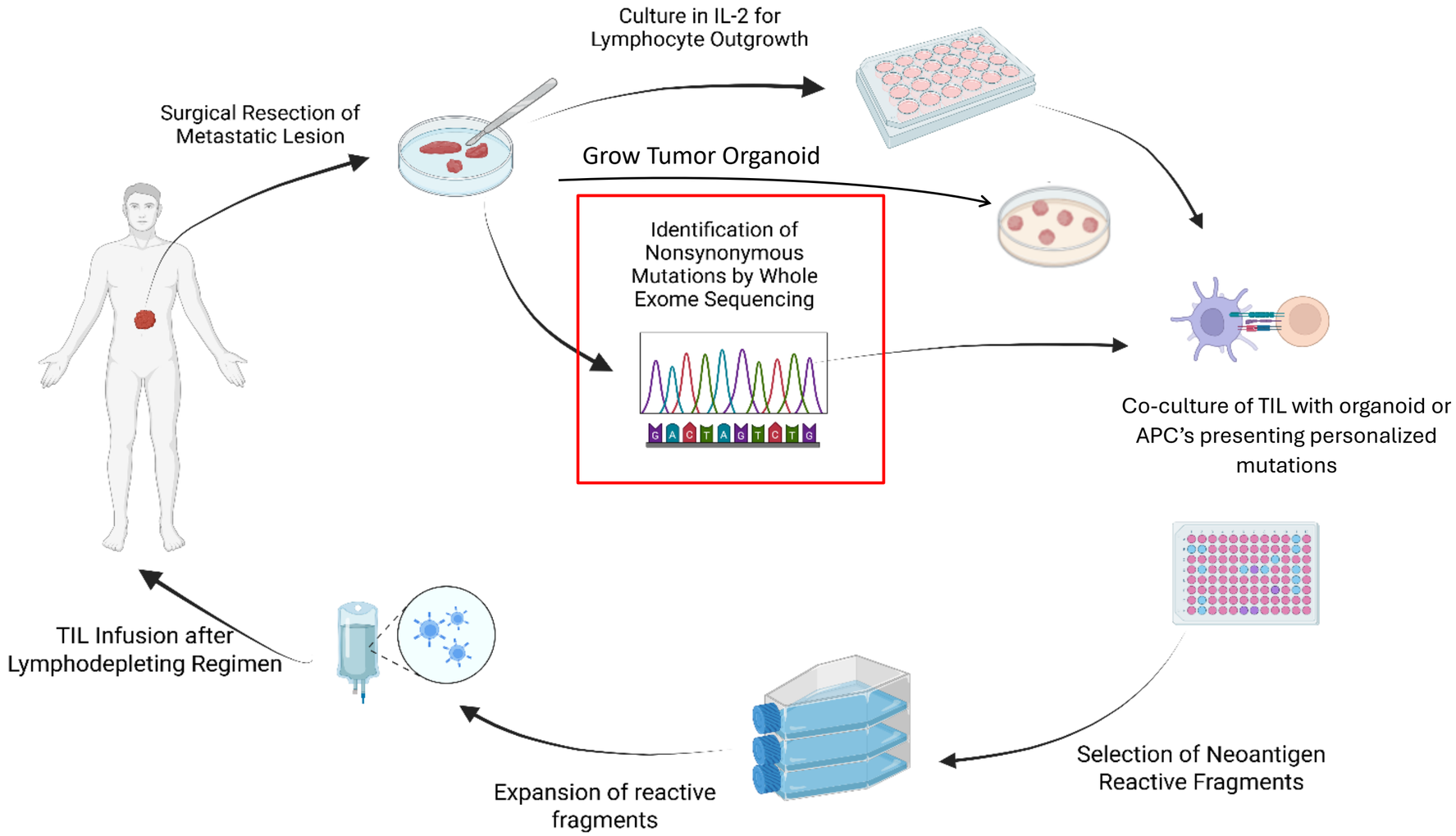
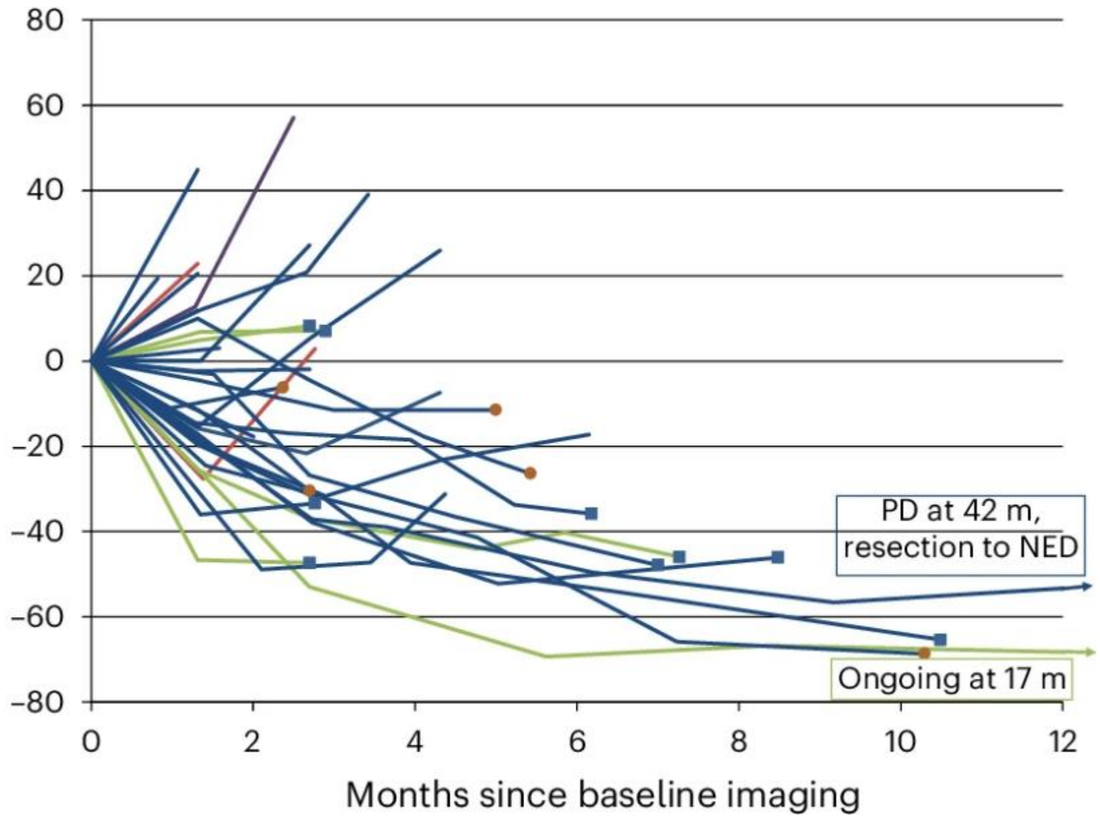
Disclosures

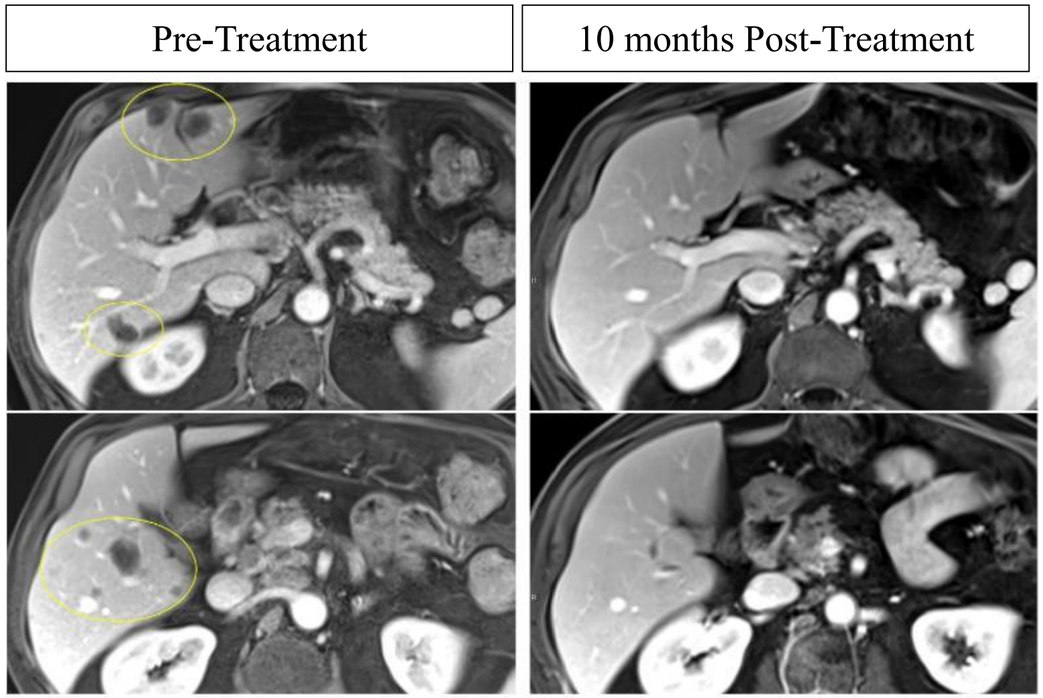
- None

TIL Growth and Neoantigen Screening



Clinical Response to TIL in Metastatic Epithelial Cancers





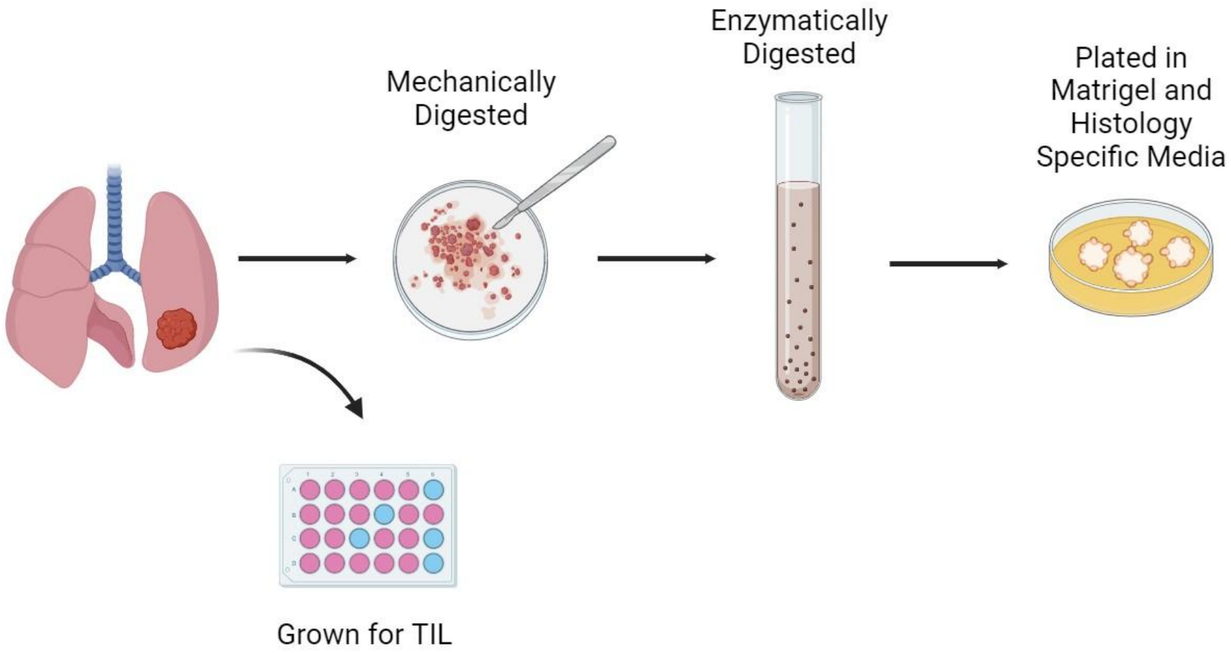
Lowery, F.J., Goff, S.L., Gasmi, B. *et al. Nat Med* (2025)

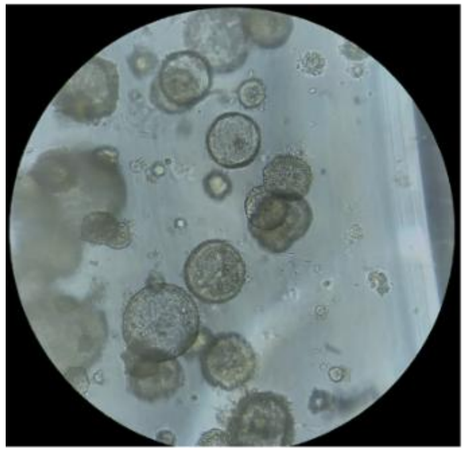
Patient Characteristics

- 30 patients treated with TIL
- Median Age 46 (40 - 54)
- 15 patients (50%) female
- Primary Diagnosis
  - Colorectal Cancer: 20
  - Pancreatic Ductal Adenocarcinoma: 4
  - Ductal Carcinoma of Breast: 2
  - Cholangiocarcinoma: 1
  - Ovarian Adenocarcinoma: 1
  - Esophageal Adenocarcinoma: 1
  - Fibrolamellar HCC: 1
- Site of TIL/PDTO Harvest
  - Lung: 20
  - Liver: 5
  - Omentum: 3
  - Abdominal Wall: 2

*more than one organoid grown from same harvest site
‡ Organoid grown from adjacent abdominal wall implant

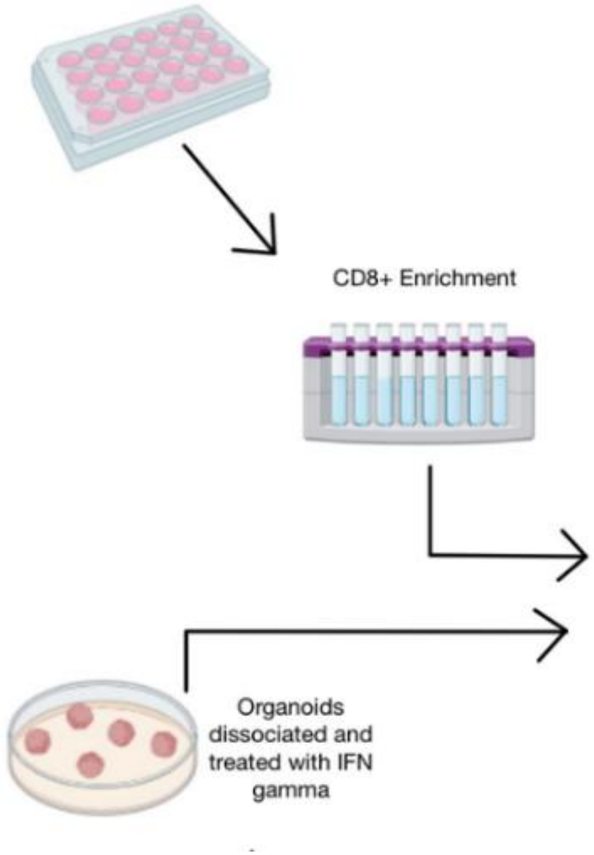
Patient Derived Tumor Organoids

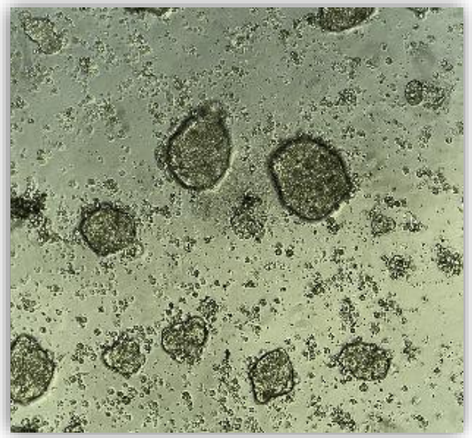




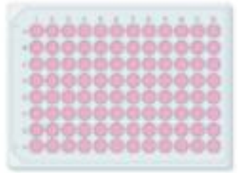
Experimental Overview

Infusion Bag (T cells) thawed

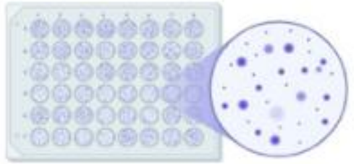




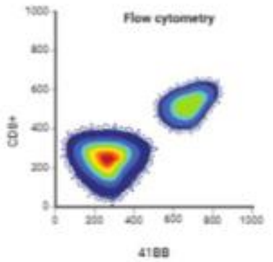
Overnight Coculture



IFN Gamma ELISpot



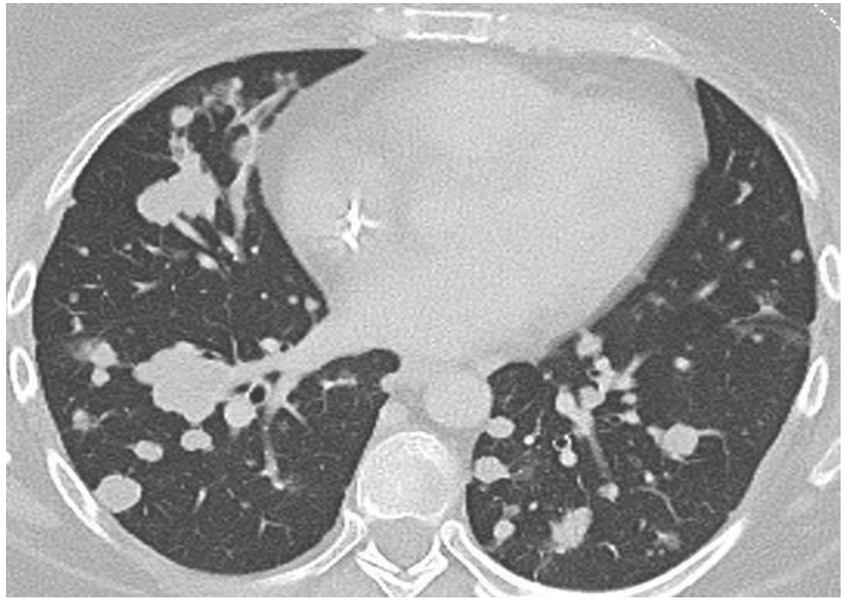
41BB Flow Analysis



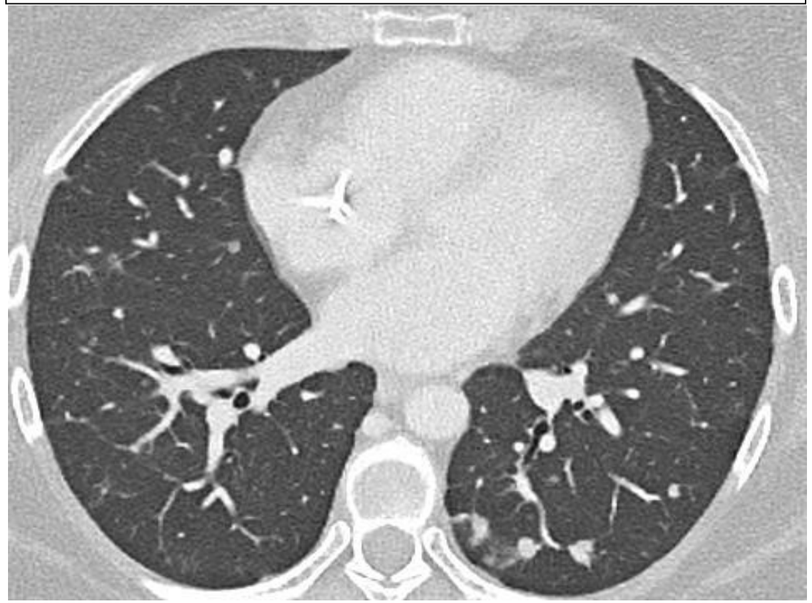
Clinical Responder

44-year-old female with metastatic colon cancer to lungs and liver
TIL harvested and organoid grown from lung lesion
Received 88e9 T cells (27% CD8+)

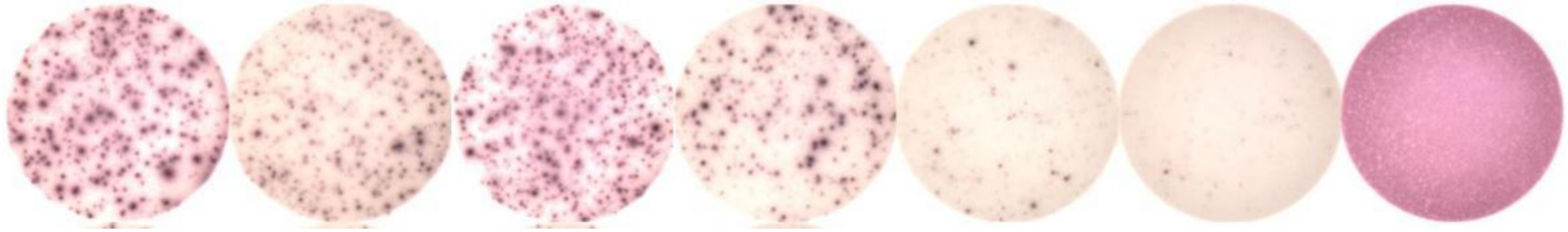
Pre-Treatment



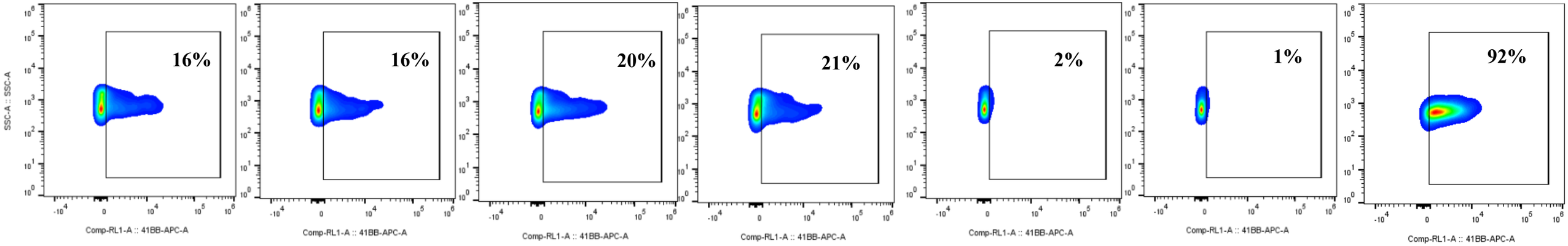
11 months Post Treatment



Responder Co-culture Results



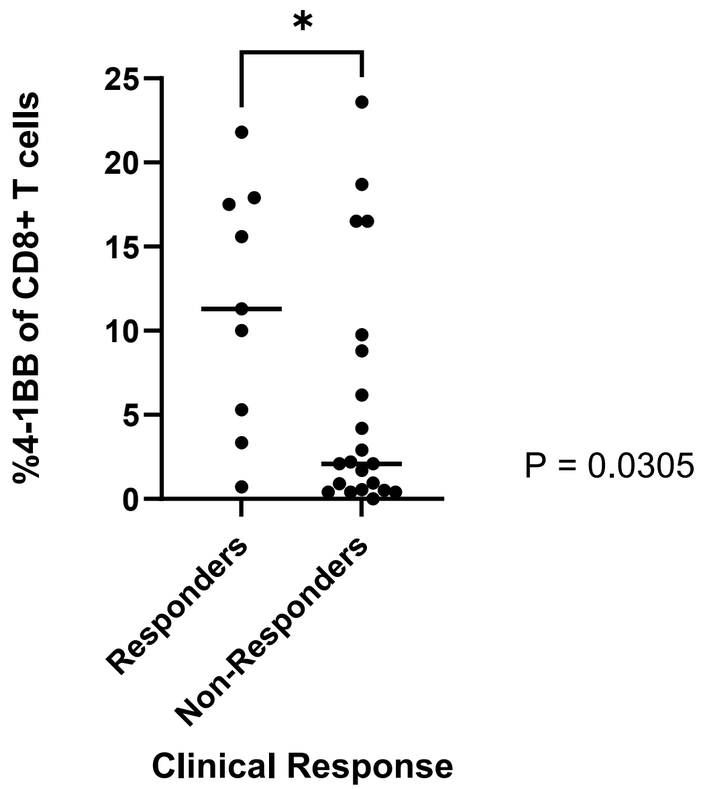
Autologous Organoid #1	Autologous Organoid #2	Autologous Organoid #3	Autologous Organoid #4	Allogeneic Organoid	T cells alone	PMA/Io



Organoid Reactivity by Clinical Response (RECIST v1.0)

	Objective Responders	Non-Responders	Objective Response Rate
TIL Infusion Reactive with Organoid	8	7	**53%**
TIL Infusion Not Reactive with Organoid	1	14	**7%**
			P=0.014

Average CD8+4-1BB% of Autologous Organoid Coculture Per patient



P = 0.0305

Conclusions

- Significant association between in vitro organoid recognition by TIL infusion product and clinical response to TIL
- Intra and Intertumoral heterogeneity are still not fully captured by PDTO
  - May explain patients who have organoid reactivity but do not have a clinical response
- Organoids are a valuable tool to evaluate immunotherapy treatments as well as mechanisms of immune evasion by tumor cells

THANK YOU!

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