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Background

Immunotherapy brings great progress for cancers that are difficult to treat. It remains challenging to select sensitive patients upfront. PD-L1 expression, TMB and MSI/MSS status do not optimally differentiate between the sensitivity to individual immunotherapies.

We aim to improve patient stratification for immunotherapy by classification of patient-specific responses using a robust ex vivo 3D tumor testing platform

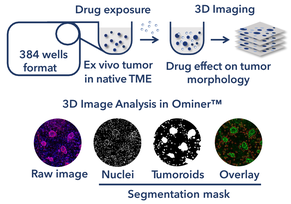
Material

Our study includes **101 patients** with predominantly ovarian carcinoma (80/101). Tumor tissue was collected in ongoing clinical trials from solids and liquids (Table 1). Five immune checkpoint inhibitors and a STING activator were tested.

Table 1: Sample characteristics

Indication	#	Tissue type	#
Ovarian	80	Ascites	65
		Solid tumor	15
Bladder (B)	8	Solid tumor	8
Lung (L)	4	Pleural fluid	4
Breast	3	Pleural fluid	2
		Biopsy	1
Mesothelioma (M)	3	Pleural Fluid	3
Melanoma	2	Cell line	2
Cervix	1	Solid tumor	1

Figure 1: Assay pipeline



Method

Fresh tumor clusters were seeded into 384 well plates and exposed to different immunotherapies, while preserving the tumor micro-environment. In parallel, clusters were treated with chemo- and targeted therapies (not shown). Tumor killing and immune cell proliferation were measured using 3D image analysis (Figure 1). Sample and result quality are ensured through extensive automated quality control, combined with manual inspection by experts.

Ex vivo tumor sensitivity was classified as no response (<10%), weak (10-20%), strong (20-50%) and very strong (>50%), based on percentage tumor killing. Its statistical significance is expressed in two categories: significant (p-value: * < 0.05) and highly significant (** < 3.33e-4, Bonferroni corrected).

Results

Differential patient response profiles were observed (Main figure and Table 2).

For the current dataset, we measured a **highly significant immunotherapy response in ~35%** of the samples. **The assay has a technical success rate of 89%.**

Table 2: Immunotherapy response

	All samples		SEA responders			
			Total		Highly significant response* (p < 0.00033)	
Treatments	Samples	Response	Samples	Response	Samples	Response
SEA *Superantigen*	101	**48.5 %**	49	100 %	37	**75.5 %**
CD3-CD28 beads	17	**47.1 %**	9	88.9 %	4	**44.4 %**
Pembrolizumab	85	**16.5 %**	42	33.3 %	8	**19.1 %**
Nivolumab	70	**10.0 %**	32	21.8 %	4	**12.5 %**
Atezolizumab	64	**12.5 %**	34	23.5 %	6	**17.7 %**
Ipilimumab	93	**19.4 %**	48	37.5 %	11	**22.9 %**
Durvalumab	48	**2.1 %**	25	4.0 %	0	**0 %**
ADU-S100	62	**37.1 %**	31	74.2 %	19	**61.3 %**

Conclusion

This study reports the development of a robust ex vivo tumor testing platform that classified patient-specific sensitivity to 6 immunotherapies in over 100 patients, demonstrating the potential of ex vivo tumor testing to optimize patient stratification for immunotherapy.

Discussion

The platform enables better selection of patients in clinical trials for novel immunotherapies and in daily practice for those who could profit from immunotherapy, thereby avoiding toxicity in those who are not sensitive for these therapies. Clinical trials are ongoing to establish the correlation of our testing with **clinical** response to immunotherapy.

SCAN ME

VitroScan
PREDICTING TREATMENT OUTCOME

LUMC Leids Universitair Medisch Centrum

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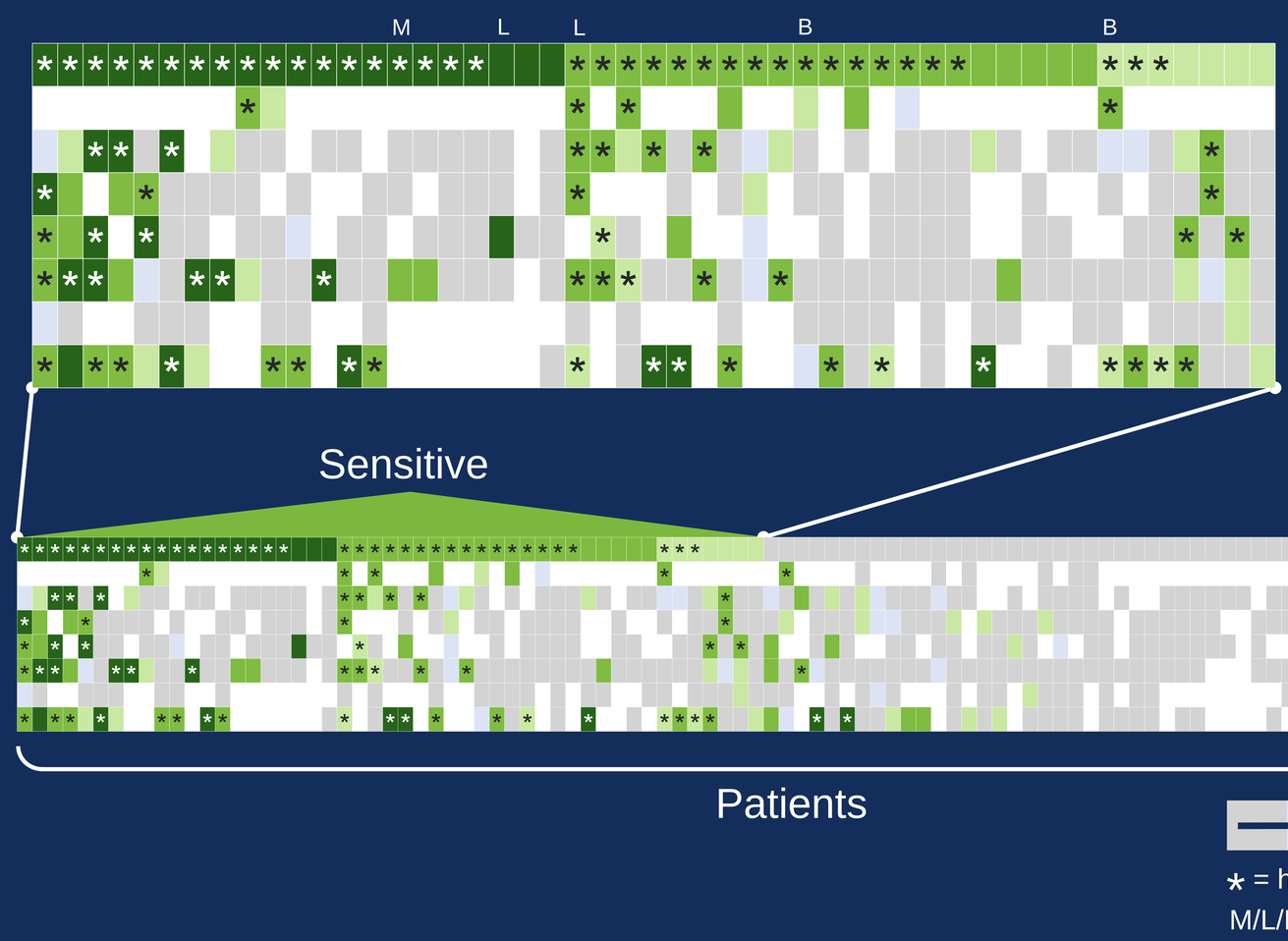
Ex-vivo 3D functional assay enables **patient-specific immunotherapy response classification**



Study of 100+ patients displays **highly significant immunotherapy response profiles** for 35% of the patients tested