Multiomic Analysis of Cutaneous Squamous Cell Carcinoma (cSCC) and Association with Response to Anti-PD1 Therapy (PD1)

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Background

- PD1 induces a durable response in advanced cSCC, still, about 30% patients are resistant to PD1.[1]
- Multi-omics analysis (tumor mutational burden [TMB] and gene expression profiling [GEP]) has shown predictive value for PD1 response in various cancer types.

Objectives

- To investigate the association between different omics and response to PD1 in patients with cSCC.

Methods

- cSCC patients were prospectively enrolled in the PIP-PREDICT study (NCT06536257)
- Baseline tumor tissues were sent for
  - TSO500 DNAseq (NGS)
  - NanoString Pancancer 360IO (GEP)
- Baseline characteristics and clinical outcomes were collected
- Patients treated with PD1 were categorized as responders or non-responders based on RECIST 1.1. Patients with stable disease were further categorized into responders/ non-responders based on PET response (PERCIST).

Results

Table 1: Baseline characteristics

N=26 (~03 Jan.2025, median follow-up 27 months)	
Gender, male	19 (73%)
Median age (range)	79 (39-98)
Immunosuppressed	4 (15%)
Head and neck primary	14 (54%)
Initial stage	I=4 (15%), II=5 (19%), III=8 (31%), IV=9 (35%)

Fig 1: Best response to PD1 per RECIST1.1

Results

Antigen presentation, T-cell, NK-cell, and immune activation are upregulated in responders. Metabolism, hypoxia and vasculature are upregulated in non-responders.

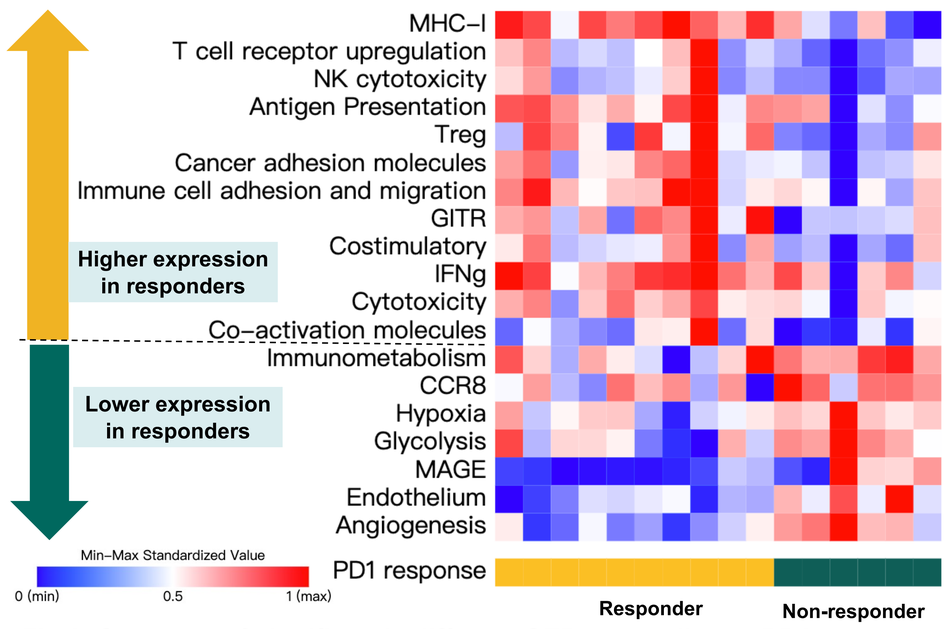

Fig 2: Summary of significantly different GEPs according to PD1 response

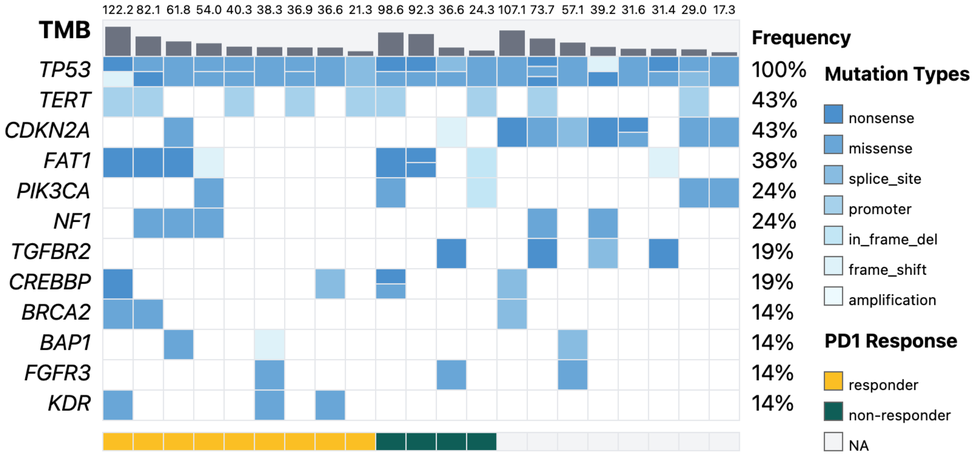

Fig 3: Summary of genetic alterations (N=21)
TMB was not significantly associated with response (p=0.64).

- Responder (Median TMB 40.3 mut/Mb (21.3-122.2).
- Non-responder (Median TMB 64.45 mut/Mb (24.3-98.6).

Key GEP differences related to primary site/ host immune response

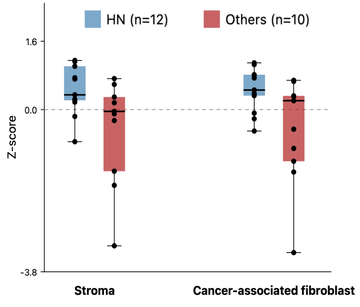

Fig 4: Head and neck primary vs others

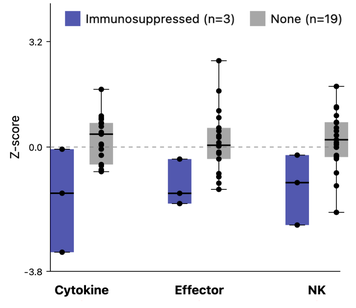

Fig 5: Immunosuppressed vs none

Conclusions

- **PD1 responders: ↑immune ↓stromal ↓hypoxia signatures.**
- **TMB and gene expression of immune checkpoints are not associated with response in our cohort.**

References

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Acknowledgements

- All patients and their families
- Research funding from Melanoma Institute Australia
- Travel grant from Melanoma Institute Australia and National Taiwan University Hospital Hsinchu Branch

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