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INTRODUCTION

Pleural mesothelioma remains an aggressive cancer with limited treatment options. Immune checkpoint inhibitors benefit only a subset of patients, and reliable biomarkers of response are lacking. MicroRNAs regulate tumour and immune biology and may provide predictors of immunotherapy benefit.

Aim: To determine whether tumour miRNA expression predicts pembrolizumab response and reflects immune microenvironment modulation in PM.

METHODS

1 Clinical cohort

- 45 treatment-naïve pleural mesothelioma tumours
- Pembrolizumab-treated patients
- 15 adjacent normal lung controls

2 miRNA profiling

- RT-qPCR of 6 candidate miRNAs
- miR-23a, miR-27a, miR-30b, miR-32, miR-155, miR-195

3 Clinical association analyses

- Best response
- Progression-free survival (PFS)
- Overall survival (OS)
- ROC and multivariable Cox models

4 Immune and pathological correlates

- CD3, CD68, CD163
- PD-L1 and BAP1

5 Mechanistic studies

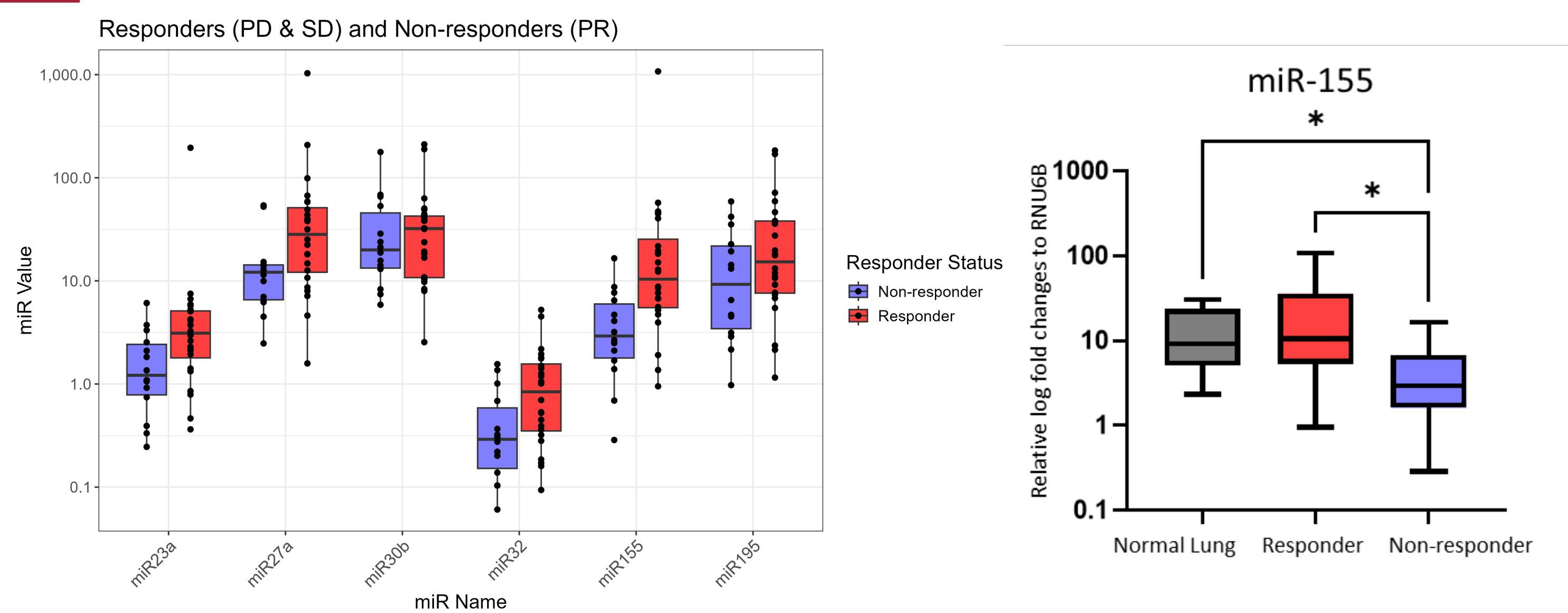
- Cell-line phenotyping and transcriptomics
- miR-155 mimic transfection (REN)
- Proliferation / clonogenicity / cell-cycle assays
- THP-1 macrophage inflammatory signalling

REFERENCES & ACKNOWLEDGEMENTS

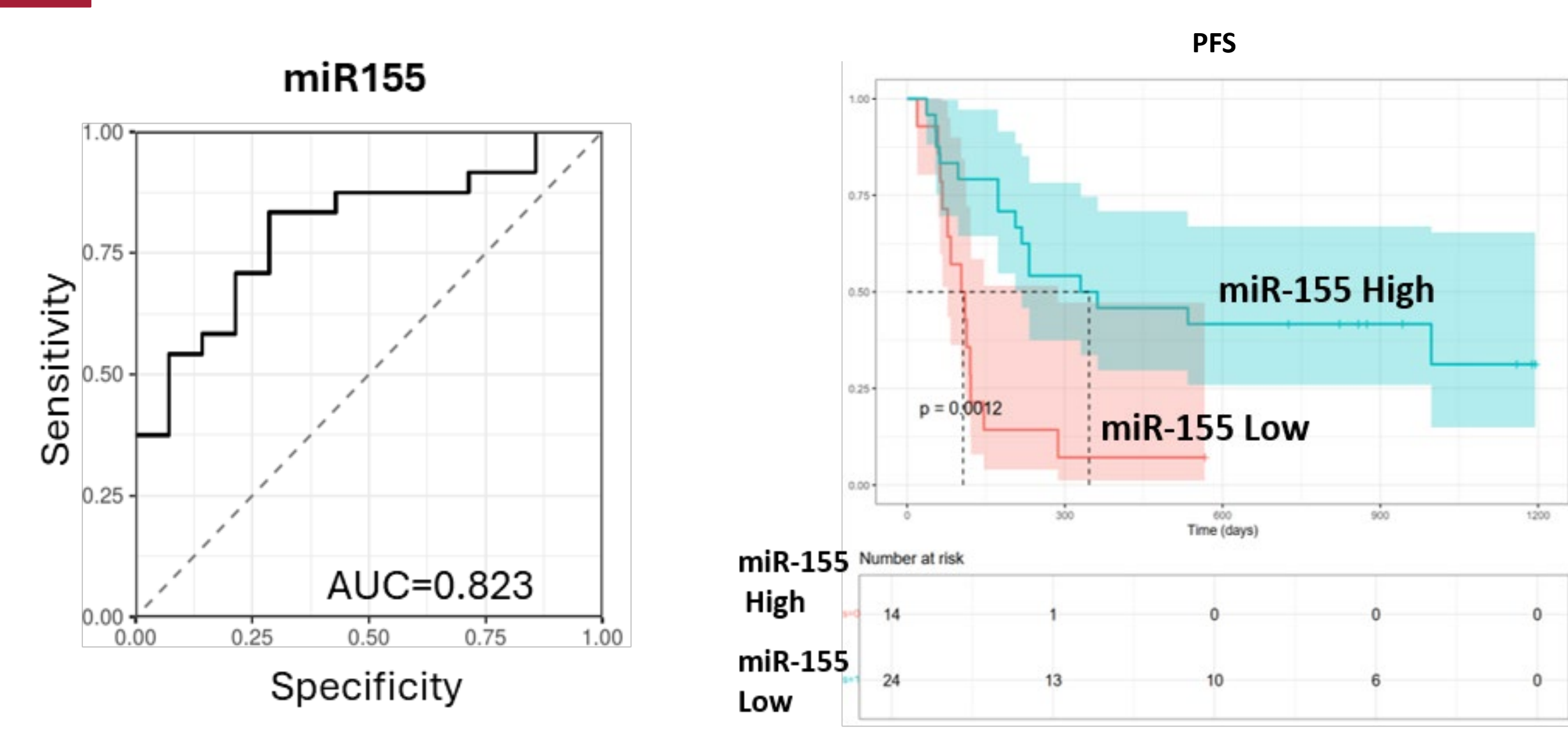
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RESULTS

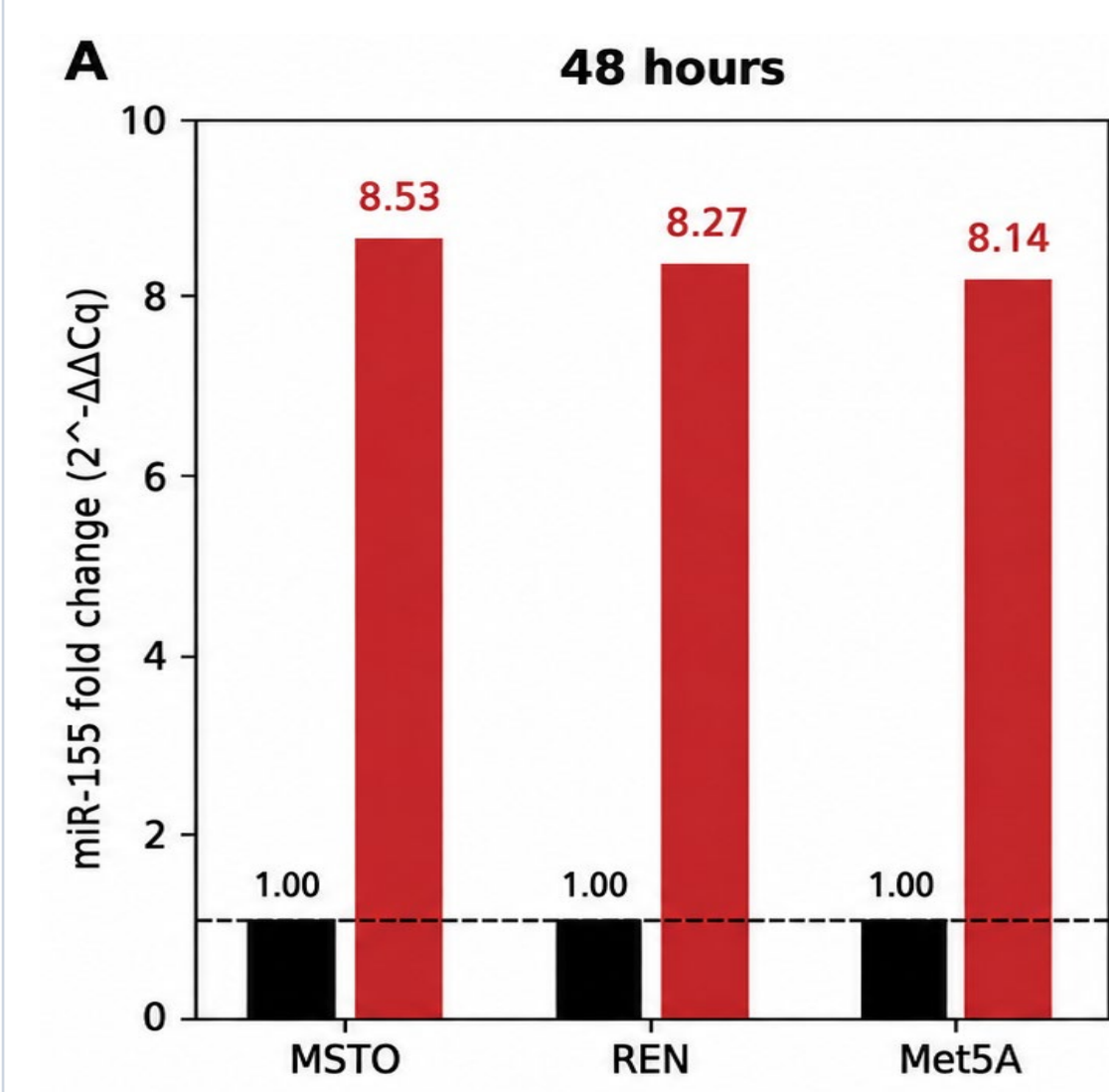
1 miR-155 is enriched in pembrolizumab responders



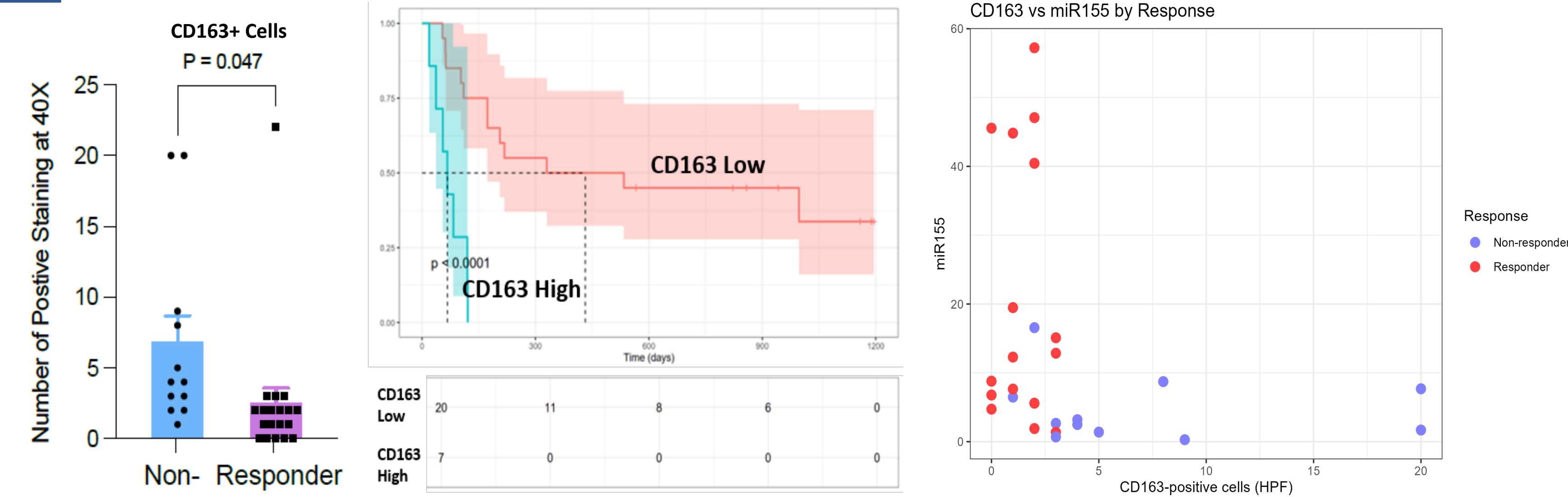
2 miR-155 predicts pembrolizumab response and survival



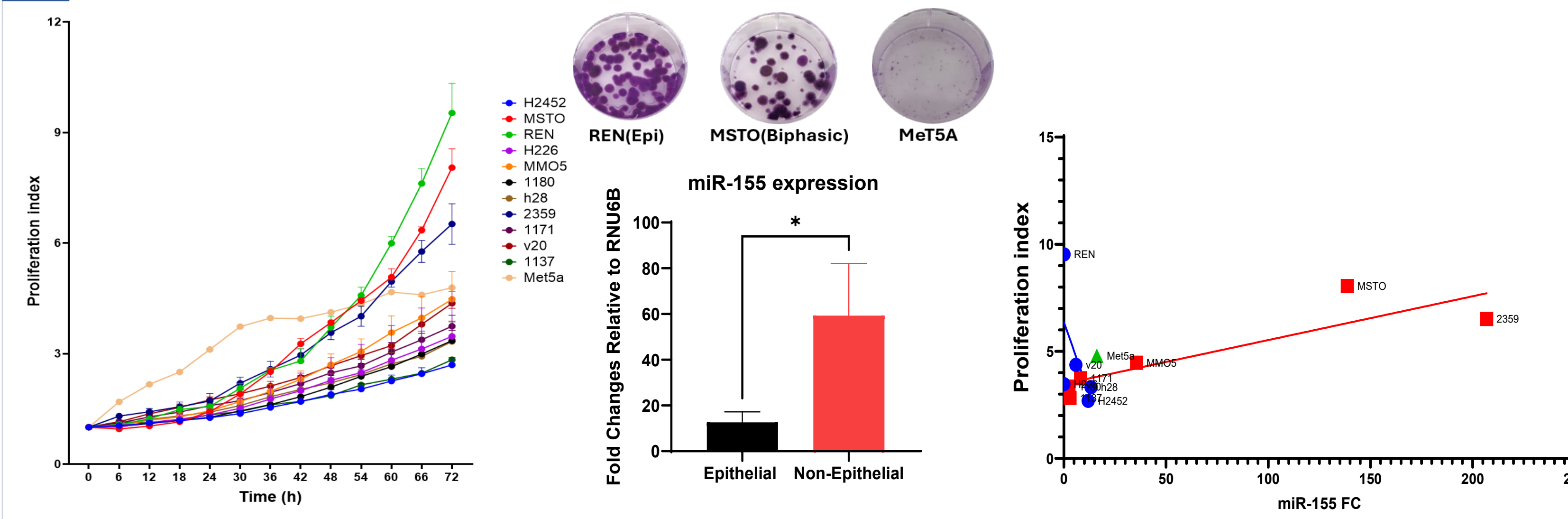
6 Robust miR-155 enrichment post transfection



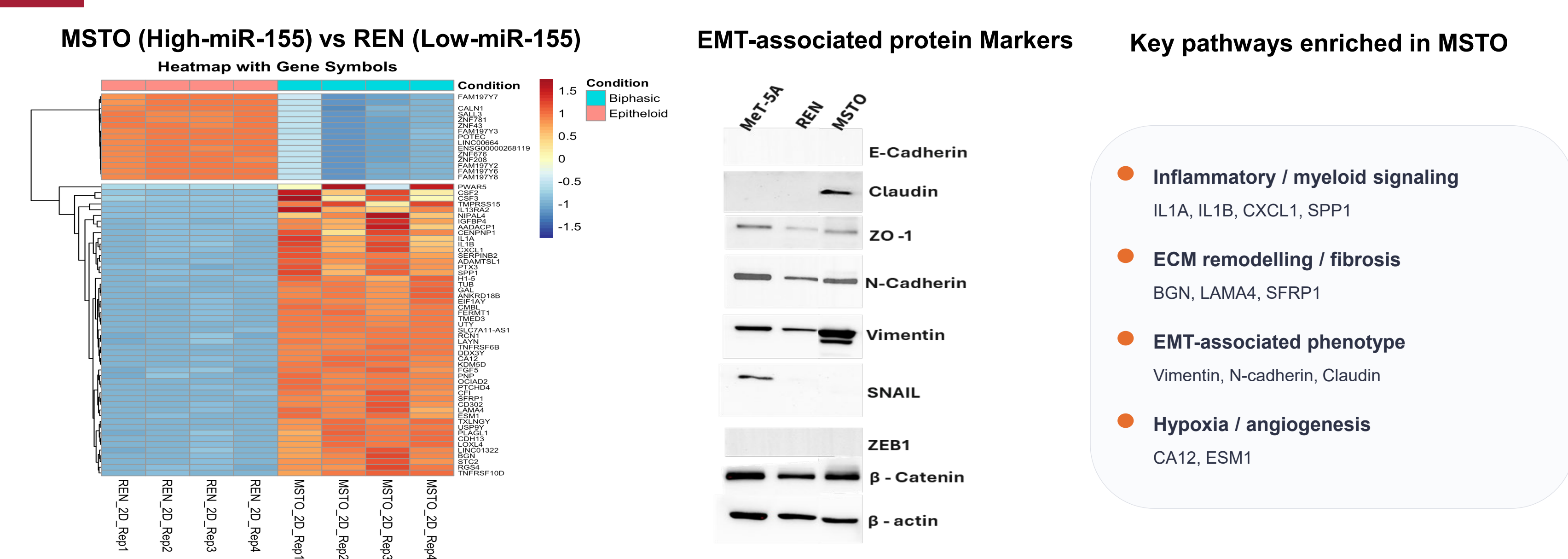
3 High miR-155 associates with lower CD163+ macrophages and improved PFS



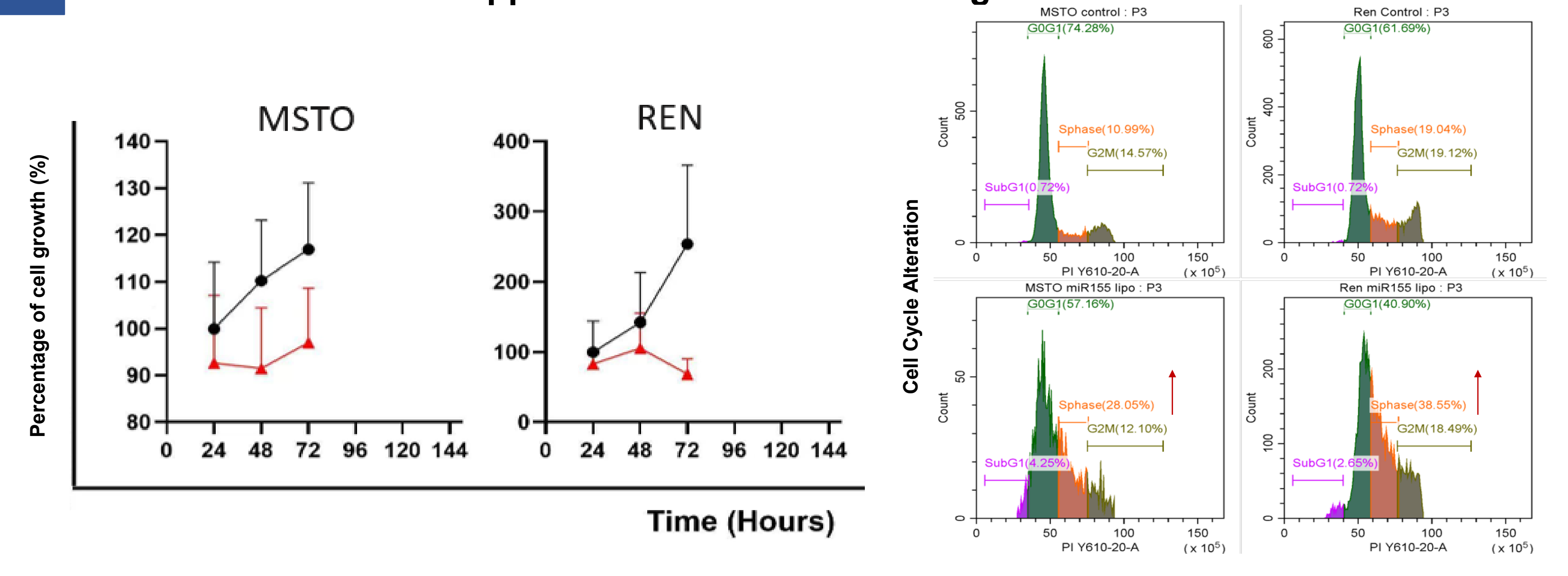
4 Mesothelioma cell lines display distinct biological phenotypes and miR-155 expression



5 High endogenous miR155 defines an inflammatory/EMT tumor phenotype



7 miR-155 enrichment suppresses mesothelioma cell growth



TAKE HOME MESSAGE & FUTURE DIRECTIONS

High tumour miR-155 is associated with pembrolizumab benefit, improved survival and lower CD163⁺ macrophage abundance.

Functional studies suggest miR-155 also modulates tumour growth and macrophage inflammatory signalling.

Future Studies

- Prospective validation of miR-155 and the multi-miRNA panel in independent PM cohorts.
- Define the mechanistic role of miR-155 in tumour-macrophage interactions and immunotherapy response.
- Evaluate whether therapeutic modulation of miR-155 can enhance immune checkpoint inhibitor efficacy.

8 miR-155-enriched tumor secretome alters macrophage inflammatory signaling

