



P2.100: Proteogenomics Reveals Distinct Pathological Subtypes of Invasive Non-Mucinous Adenocarcinoma

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INTRODUCTION

Invasive non-mucinous adenocarcinoma (INMA) shows marked histologic heterogeneity, with distinct prognostic profiles across subtypes (lepidic, acinar, papillary, micropapillary, solid). Morphology and molecular profiles are not strictly one-to-one; they may reflect probabilistic, many-to-one couplings. Prior reports link EGFR to acinar/lepidic and TP53 to papillary/solid patterns. We test whether invasive subtypes (micropapillary/solid), aggressive driver genotypes (TP53/NF1/MET/PIK3CA/FGFR1), and high CYFRA 21-1 co-cluster along a shared prognostic axis. Objective: Integrate histologic subtype, genotype, and biomarker signals to validate subtype–genotype coupling and assess its independent prognostic value.

METHODS

Cohort: 200 patients with INMA, each with comprehensive genomic, proteomic, and histologic subtype-proportion data.

Histology: Subtype proportions recorded per WHO classification; combinations constructed and merged proportions calculated.

Molecular data: Driver mutation status (EGFR, TP53, MET, NF1, PIK3CA, FGFR1) and circulating/serum biomarker CYFRA 21-1.

Statistics: Prognosis: Cox regression (univariable → multivariable adjusted for stage, age); Multiplicity: BH–FDR correction; Associations: correlation matrix with partial/point-biserial checks; expected negative correlations among mutually nested subtype proportions were accounted for; Robustness: median cut-off cross-validated against quartiles and continuous proportions.

DISCUSSION AND CONCLUSION

- **Actionable Takeaway Message**
Invasive histology (micropapillary/solid), aggressive driver mutations (TP53/NF1/MET/PIK3CA/FGFR1), and high CYFRA 21-1 co-cluster along a shared prognostic axis — integrating morphology + genotype + biomarker improves prognostic stratification.
- **Future Direction for Research**
External validation of the subtype–genotype coupling in an independent cohort
Provide an operable panel

REFERENCES & ACKNOWLEDGEMENTS

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Artificial Intelligence (AI) Use Disclaimer: No generative AI tools were used in the preparation of this manuscript

- Wechat QR code



RESULTS

- Figure 1: Top genes with the highest mutation frequency in our cohorts.
- Figure 2: Gene mutation frequency in different histologic subtypes.
- Figure 3: KM survival curves show that high CYFRA 21-1 has a bad prognosis.
- Figure 4: Correlation matrix of core biomarkers (genotype × subtype coupling).

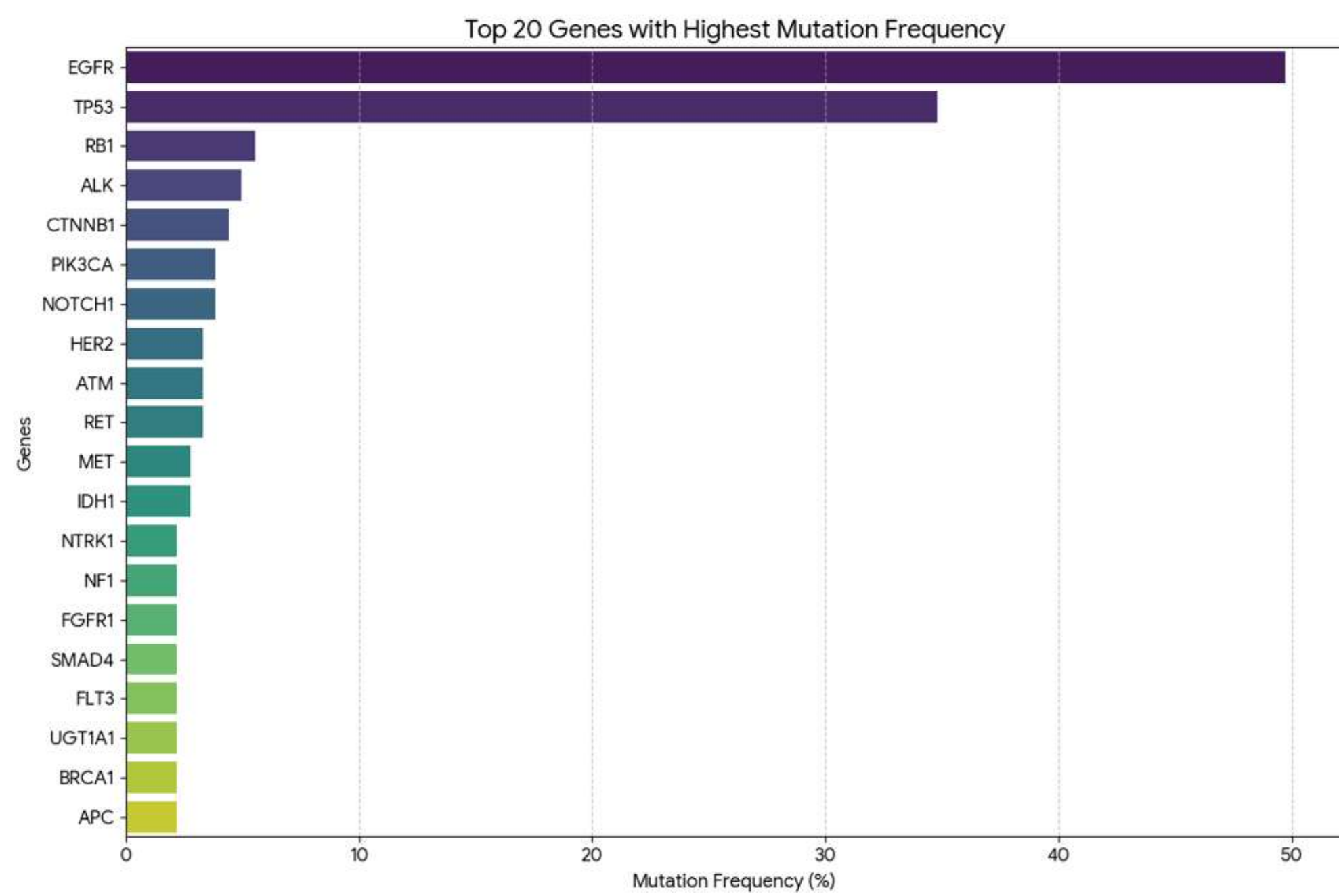


Figure 1

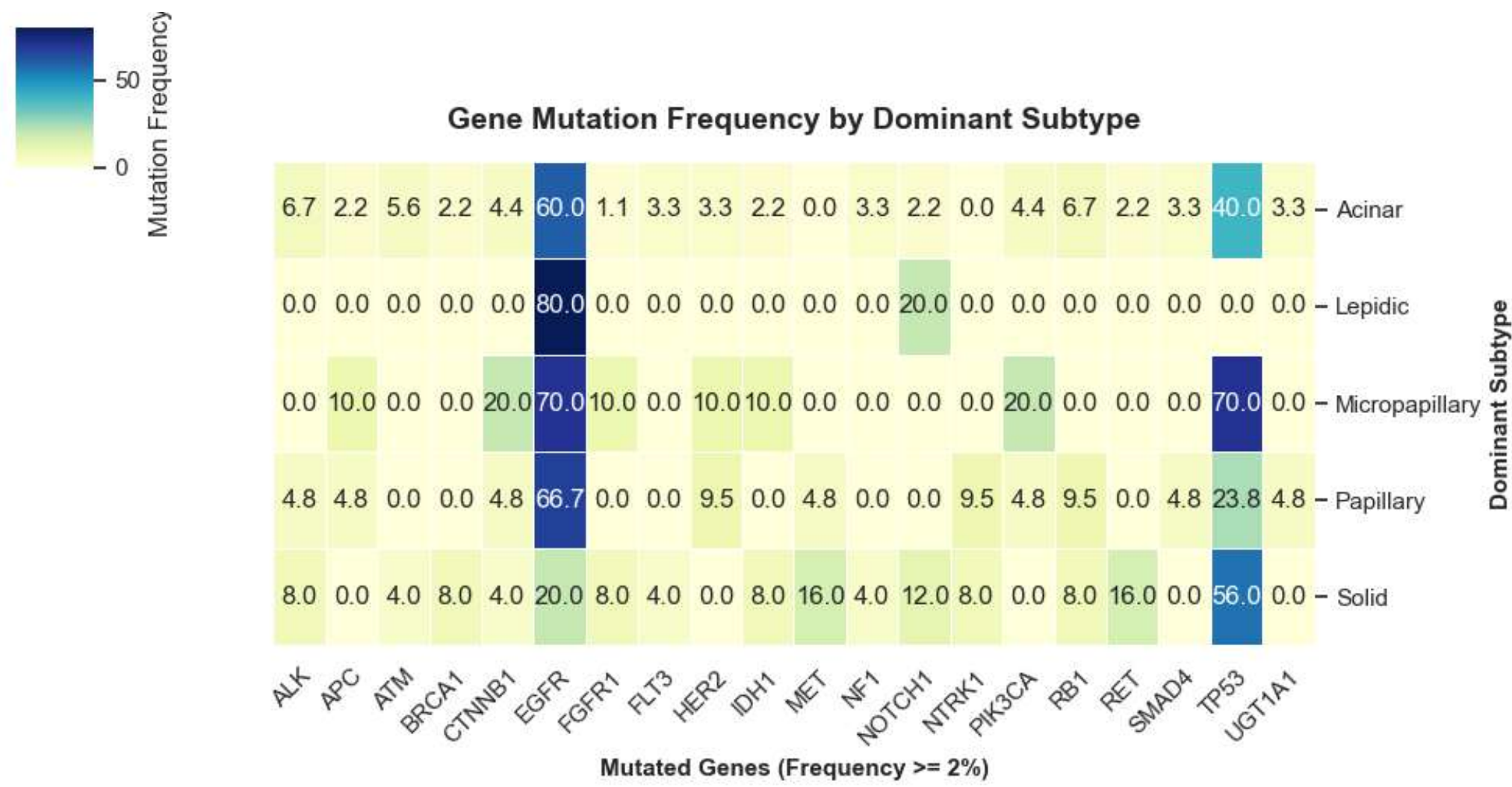


Figure 2

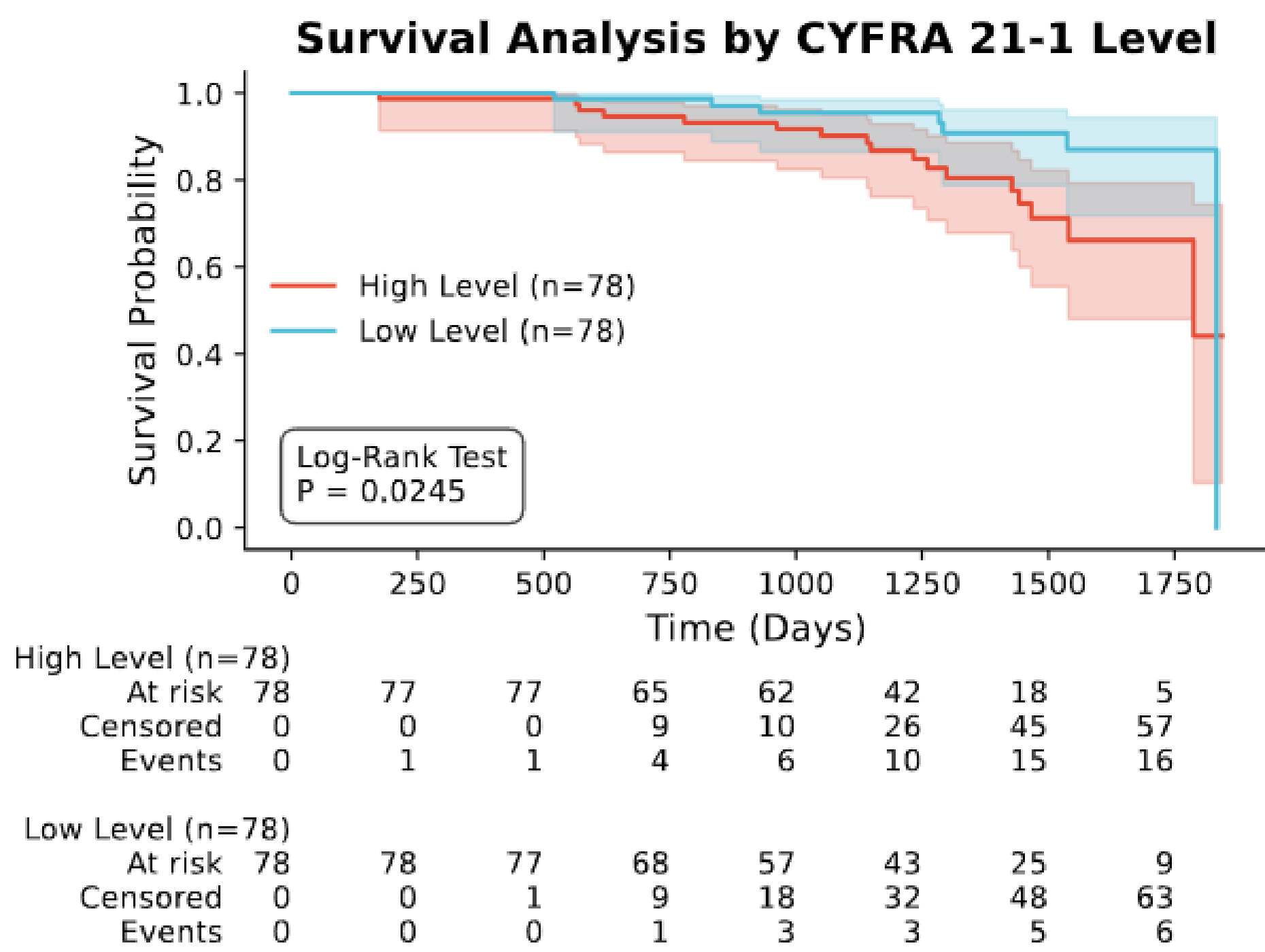


Figure 3

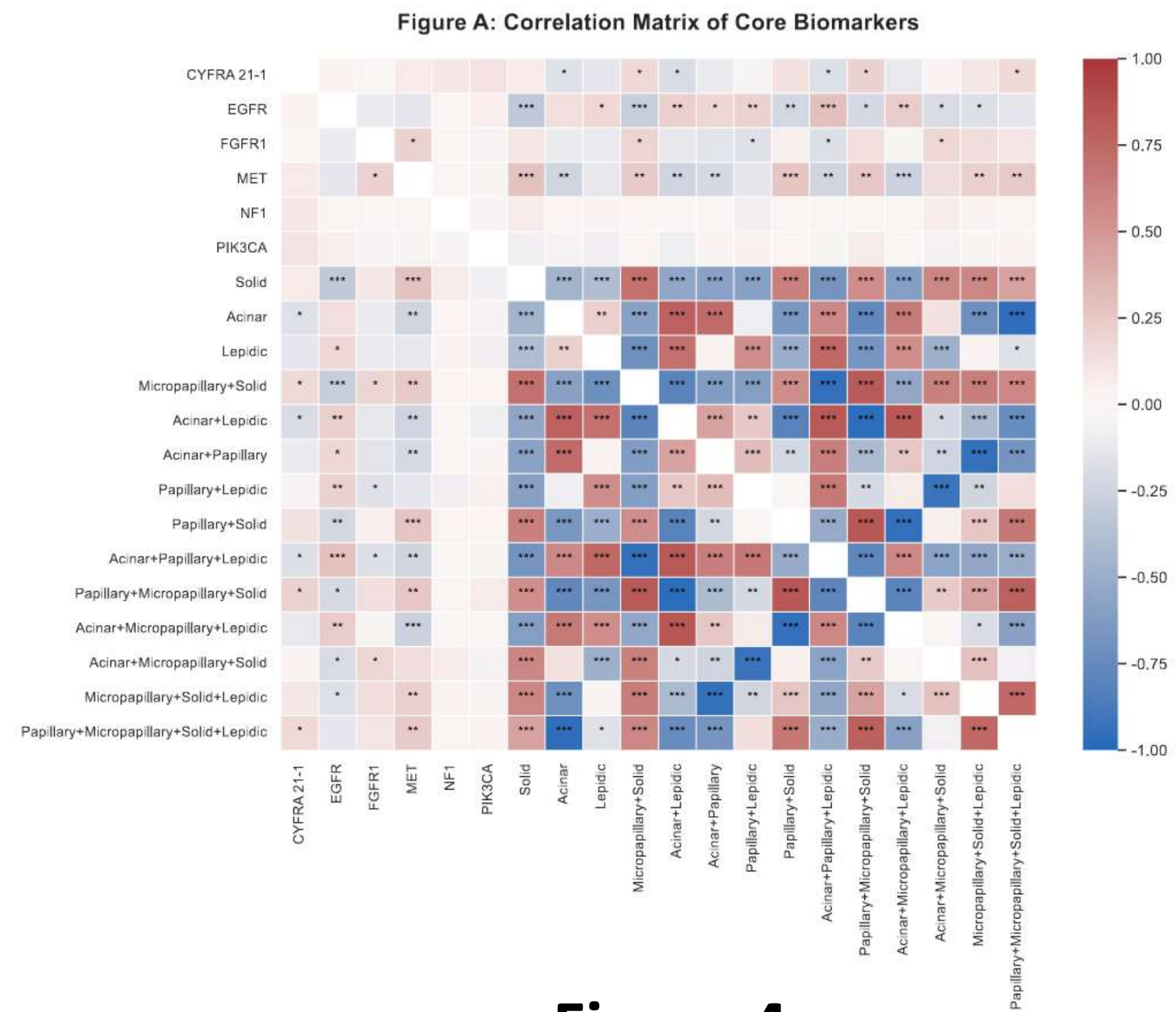


Figure 4