

Evolutionary clonality shape prognostic stratification in driver-positive NSCLCs

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INTRODUCTION

- Robust molecular signatures for predicting tumor progression remain limited in EGFR- and TP53-mutant-enriched Chinese non-small cell lung cancer (NSCLC).
- Evolutionary genomic signatures integrating recurrent driver mutations may provide a novel framework for prognostic stratification.

METHODS

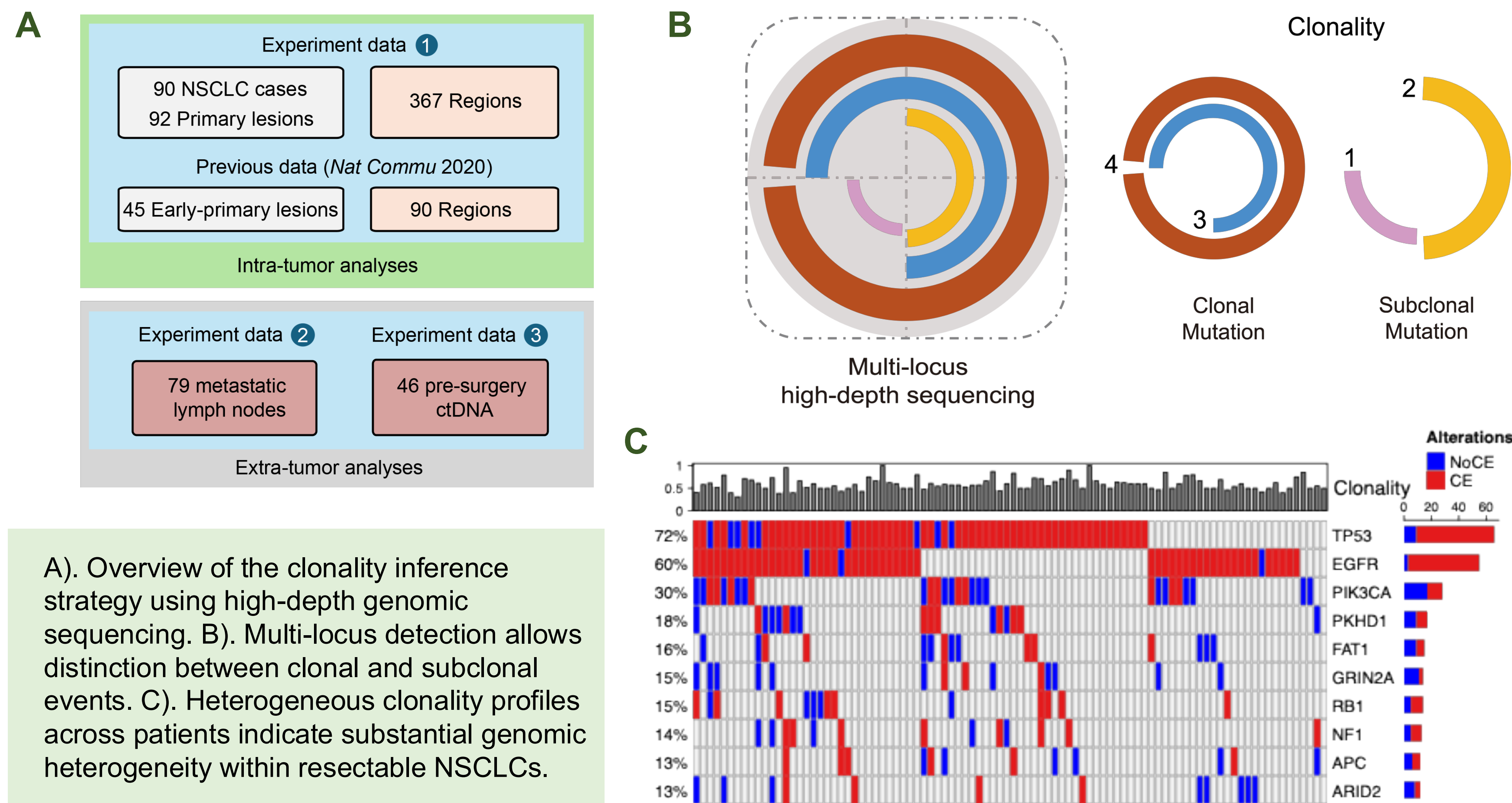
- In this cohort study, multi-region targeted genomic sequencing was performed on 367 tumor regions from 90 primary NSCLC patients, along with 79 matched metastatic lymph nodes and 46 preoperative ctDNA-positive plasma samples. A 425 cancer-related gene panel was applied with high-depth sequencing.
- For mechanistic investigation, RNA sequencing was conducted in 10 tumor samples, and multiplex immunofluorescence staining was performed in an independent cohort of 83 samples.

CONCLUSION

- Evolutionary genomic profiling represents a promising strategy for clinical risk stratification. The identification of novel evolutionary subtypes and metastasis-associated biomarkers may inform personalized therapeutic strategies for Chinese NSCLC patients.

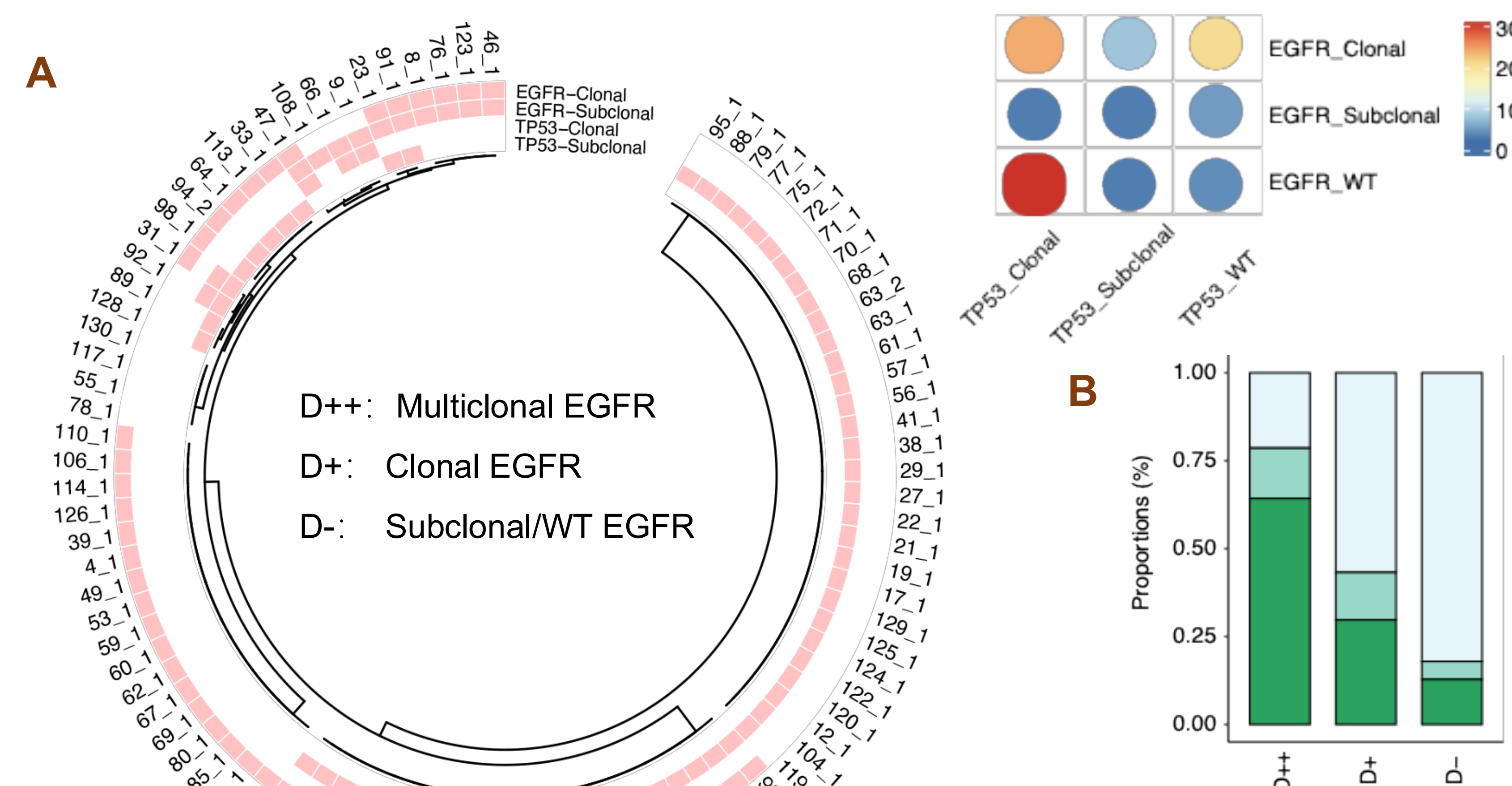
RESULTS

Figure 1. Multi-locus Sequencing for Driver Clonality and Phylogenetic Inference



A). Overview of the clonality inference strategy using high-depth genomic sequencing. B). Multi-locus detection allows distinction between clonal and subclonal events. C). Heterogeneous clonality profiles across patients indicate substantial genomic heterogeneity within resectable NSCLCs.

Figure 2. Functional clonality subtyping based on EGFR and TP53 mutations



A). Focusing on the most frequently mutated genes, EGFR and TP53, we identified distinct clonality clustering patterns. Notably, clonal and subclonal aggregation regions differed significantly. B). Clonality status of canonical driver genes was associated with clinical phenotypes.

Figure 3. Definition of the evolutionary biomarker MQMV

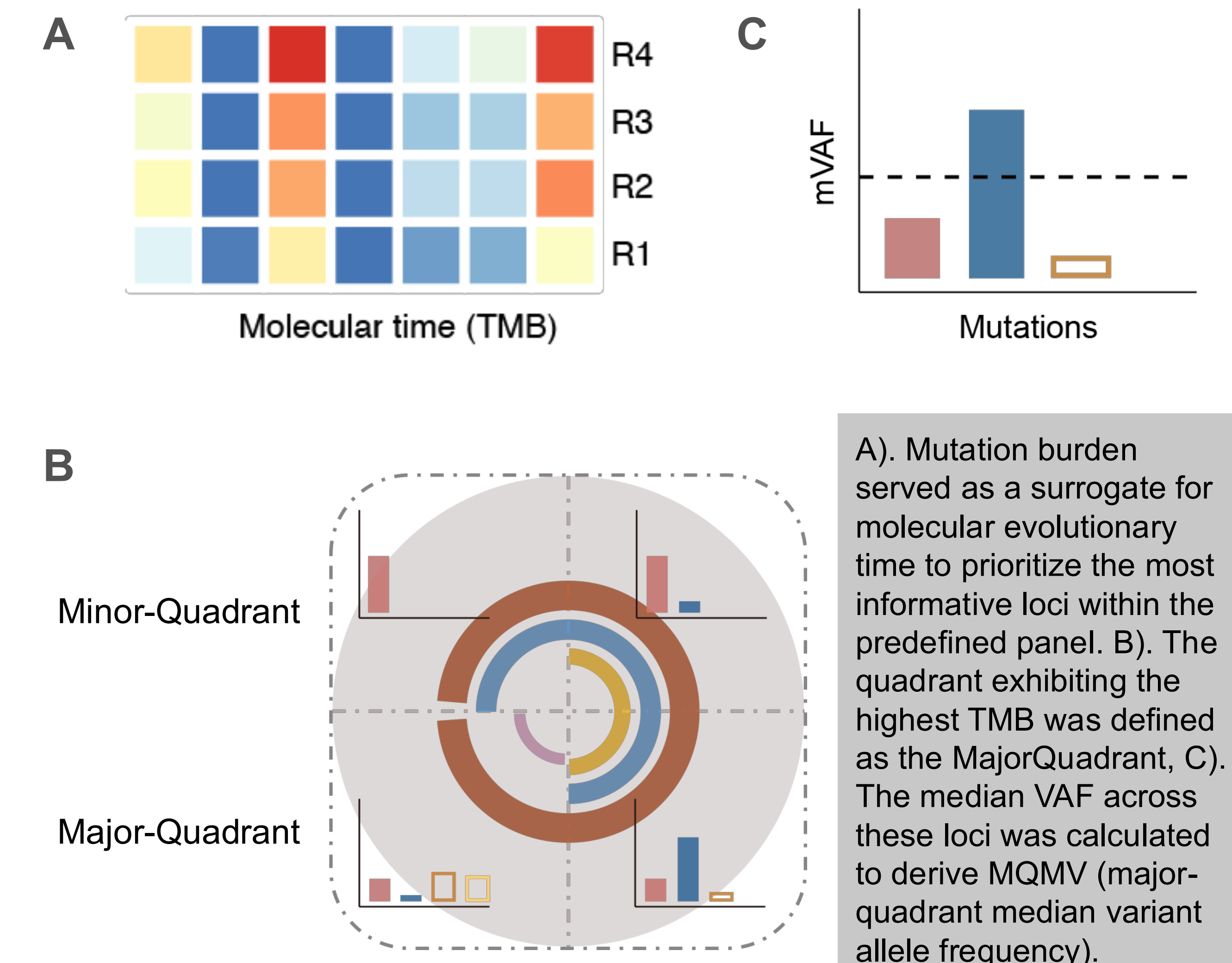


Figure 4. Prognostic stratification by MQMV across evolutionary subtypes

