



EP12.15: Enhanced Detection of EGFR PACC Mutations and Co-mutation Complexity by DNA+RNA Amplicon-Based NGS Compared With DNA Capture-Based NGS in Non–Small Cell Lung Cancer

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INTRODUCTION

- *EGFR* PACC mutations are noncanonical *EGFR* alterations with variable TKI responses.
- Detection efficacy varies by sequencing method due to their structural complexity.
- Data comparing DNA+RNA amplicon-NGS between DNA capture-NGS for PACC are limited.

Objective: compare detection rate, *EGFR* PACC variant spectrum, and co-mutation landscapes between two NGS strategies.

METHODS

STUDY DESIGN

Comparison of amplicon-based DNA+RNA co-detection versus capture-based DNA-only NGS in NSCLC

Real-world NSCLC cohort analysis

Two independent cohorts analyzed using different NGS strategies

COHORT 1

DNA+RNA co-detection cohort
n = 1,271
gene amplicon-based panel

COHORT 2

DNA-NGS cohort
n = 2,360
gene capture-based panel

SEQUENCING STRATEGY
Amplicon-based DNA + RNA

SEQUENCING STRATEGY
Capture-based DNA only

COMPARATIVE ANALYSES

Detection rate of EGFR PACC mutations
Comparison of overall detection rates between the two sequencing approaches

Variant distribution of EGFR PACC mutations
Comparison of variant spectra, including low-frequency and structurally complex mutations

Co-mutation patterns with other driver genes
Comparison of EGFR co-mutations and cross-driver co-mutations between the two approaches

OBJECTIVE
Evaluate differences in sensitivity and mutational landscape between amplicon-based DNA+RNA co-detection and capture-based DNA-only NGS in NSCLC.

DISCUSSION AND CONCLUSION

- Compared with capture-based DNA-NGS, the amplicon-based DNA+RNA co-detection approach improves the detection of *EGFR* PACC mutations, particularly for low-frequency and structurally complex variants, and enables more comprehensive characterization of co-mutation patterns.
- These findings highlight the importance of optimized sequencing strategies for accurately profiling complex *EGFR* mutations and their evolutionary trajectories, with potential implications for precision treatment in NSCLC.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

Table 1. Distribution and detection rates of *EGFR* PACC mutations by DNA+RNA amplicon-based NGS.

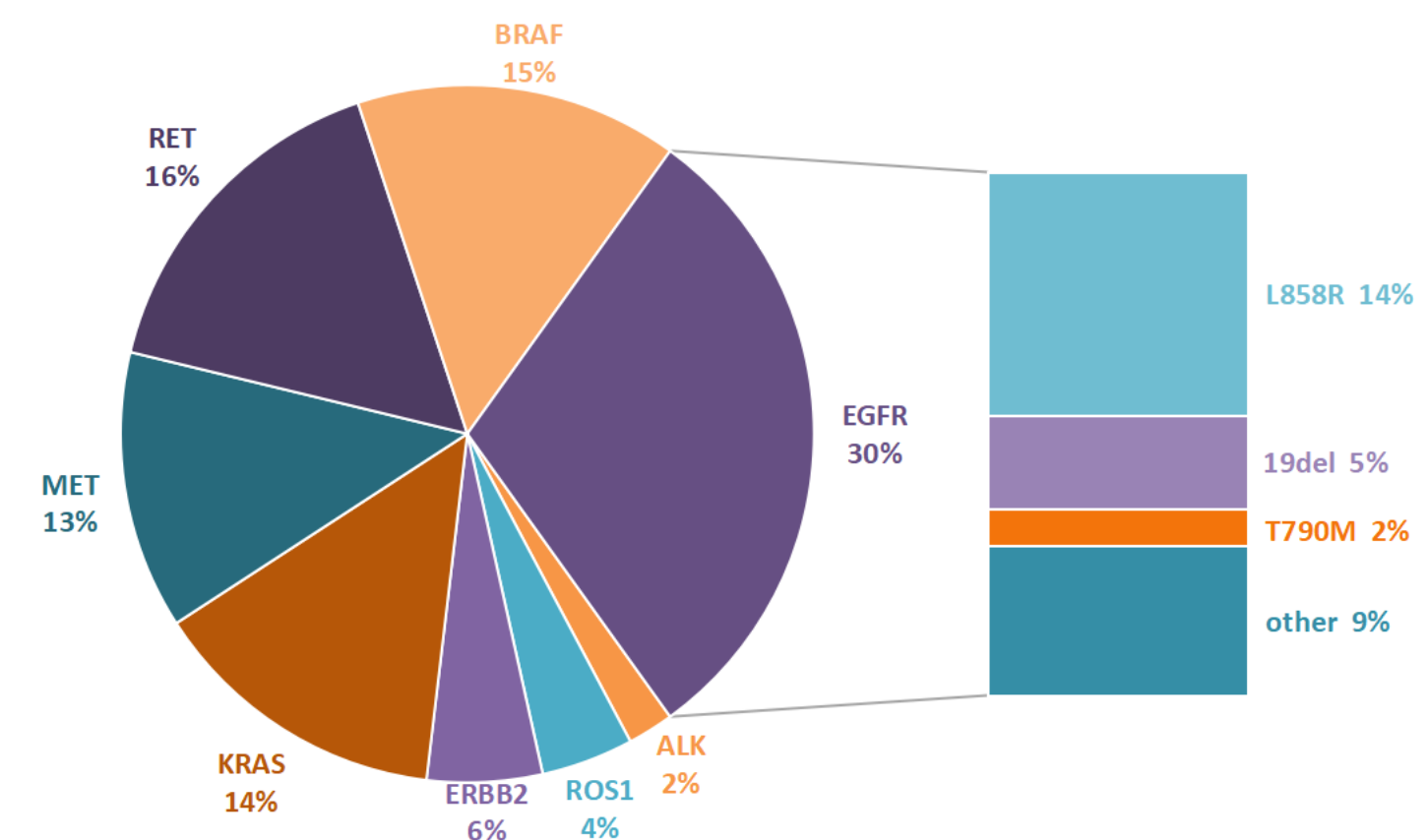
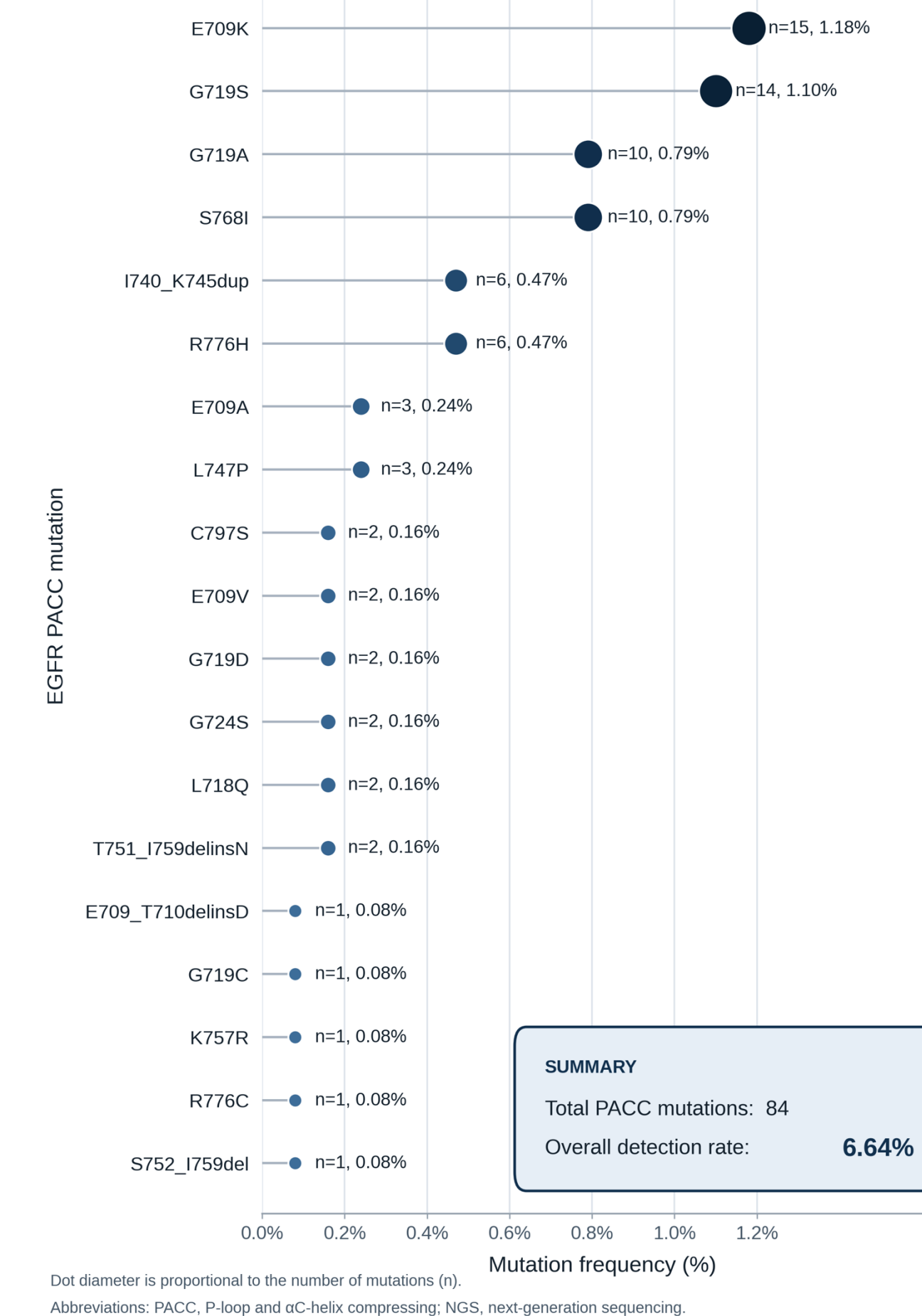


Figure 1. Co-mutation landscape of *EGFR* PACC by DNA+RNA amplicon-based NGS.

Table 2. Distribution and detection rates of *EGFR* PACC mutations by DNA capture-based NGS.

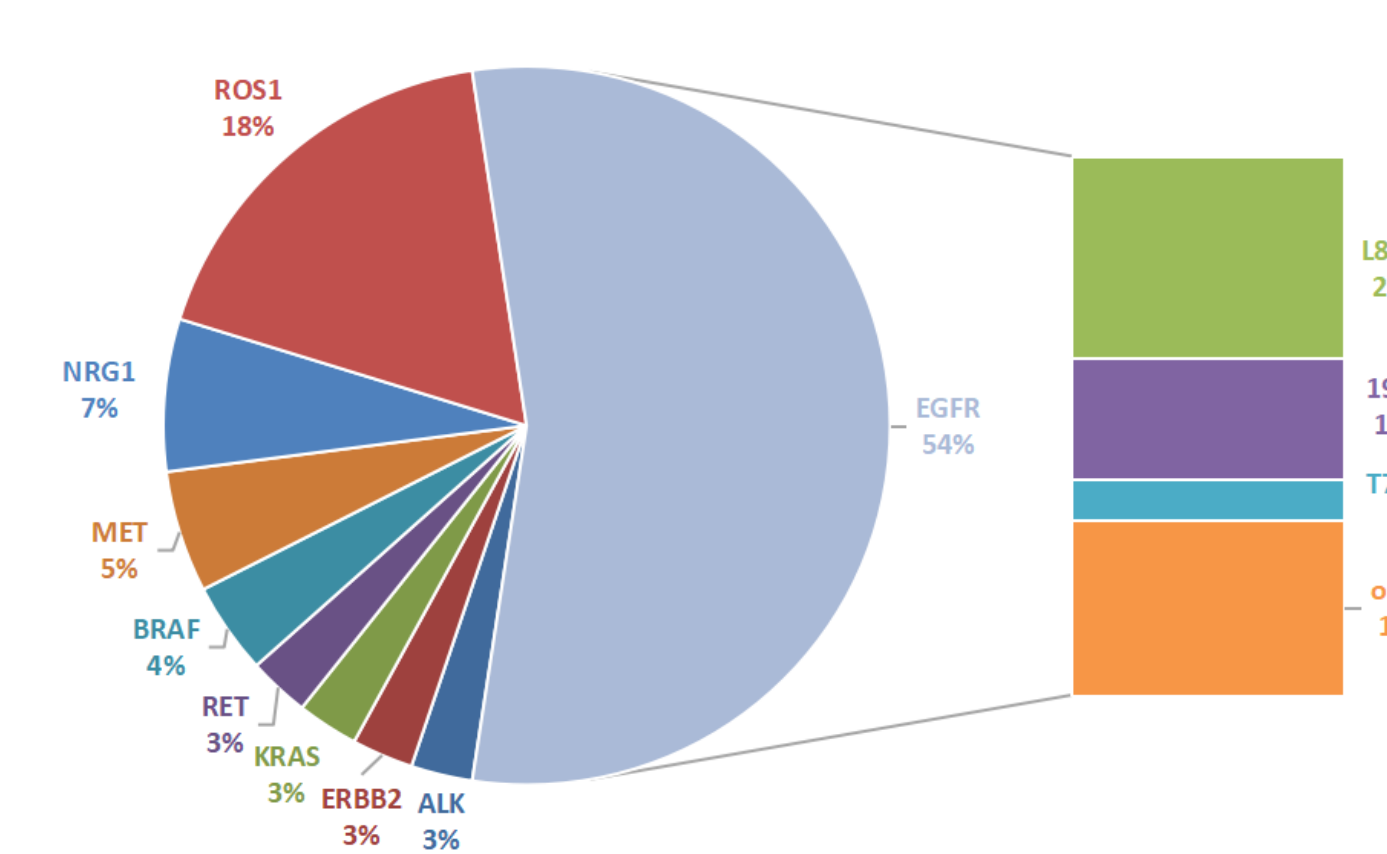
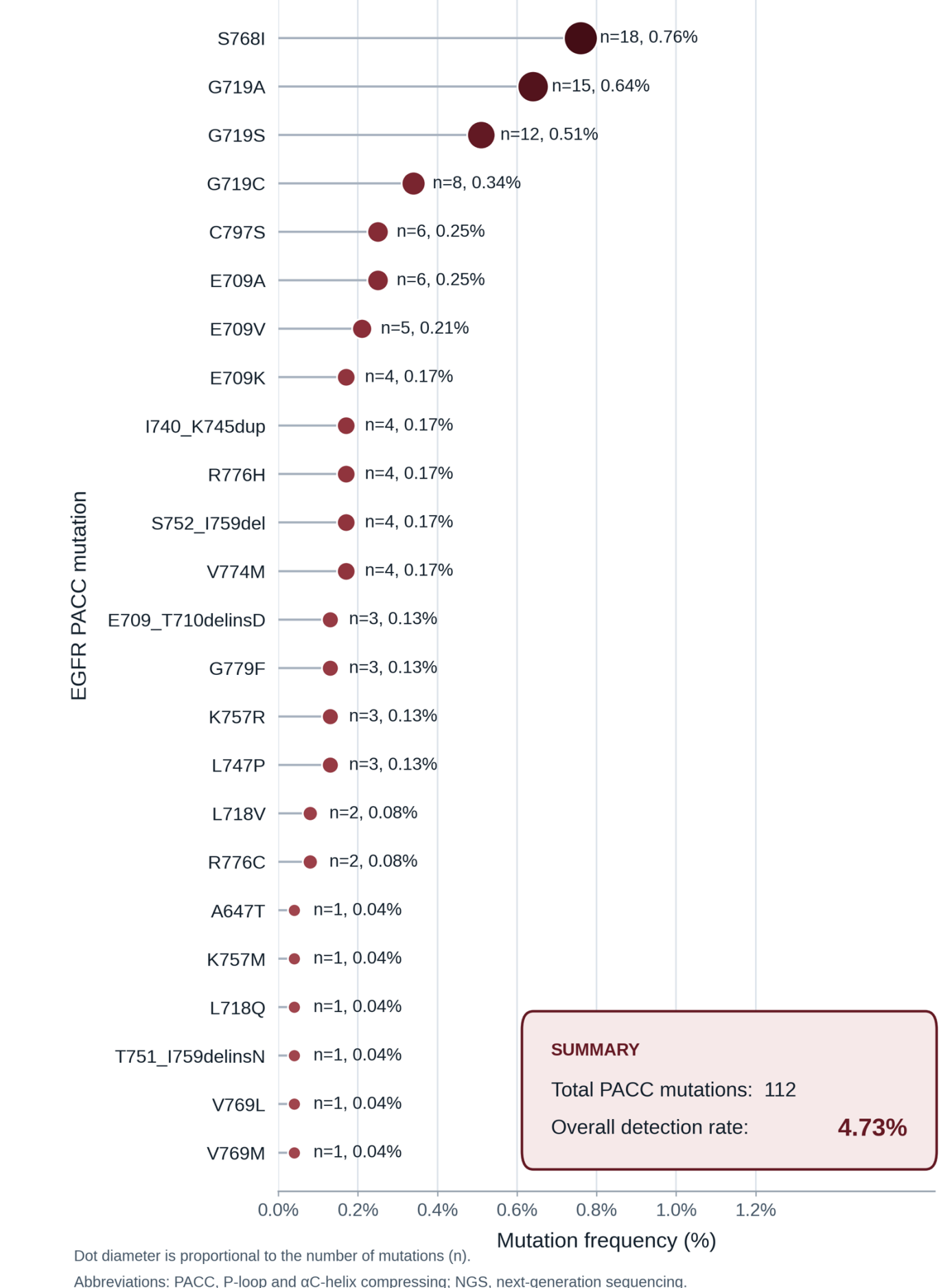


Figure 2. Co-mutation landscape of *EGFR* PACC by DNA capture-based NGS.



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