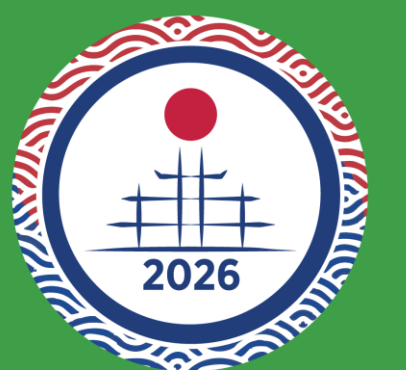


P3.262: Discovery of Drug-Response Biomarkers Using Label-Free Plasma Proteomics in NSCLC Patients Treated with JIN-A02, a Fourth-Generation EGFR-TKI

Hee-Yeon Kim¹, Sun Min Lim², Wookyoung Yu³, Seong-Kyoon Choi⁴, Anna Jo⁵, Ethan Seah⁵, Choonok Kim⁵, Sehyeon Han⁵, Jaelim Cho⁶, Byoung Chul Cho²

¹ Core Protein Resources Center, Daegu Gyeongbuk Institute of Science & Technology (DGIST), Daegu, Republic of Korea; ² Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; ³ Department of Brain Sciences, Daegu Gyeongbuk Institute of Science & Technology (DGIST), Daegu, Republic of Korea; ⁴ Division of Biomedical Technology, Daegu Gyeongbuk Institute of Science & Technology (DGIST), Daegu, Republic of Korea; ⁵ J INTS BIO Inc., Seoul, Republic of Korea; ⁶ Department of Preventive Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea



IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- Epidermal growth factor receptor (EGFR) mutations are the predominant drivers of NSCLC. While EGFR tyrosine kinase inhibitors (TKIs) are the primary treatment for EGFR-mutant NSCLC patients, resistance inevitably develops, leading to disease progression.
- JIN-A02, a novel 4th generation EGFR-TKI, intended for oral administration, selectively and reversibly binds to EGFR mutations, including the C797S and/or T790M mutation that causes resistance to 3rd generation of EGFR-TKIs.
- This study was conducted to discover proteomics-based biomarkers using plasma samples from subjects receiving JIN-A02, which is currently in Phase 1/2 Clinical Trial (NCT05394831).

Methods

- Twenty-five longitudinal plasma samples were collected from patients with NSCLC treated with JIN-A02 at pre-treatment and during therapy, including time points aligned with clinical response assessments between Cycles 2 and 9. In addition, 60 plasma samples from healthy controls were included as reference samples for cross-sectional proteomic comparison. Following plasma protein preparation, LC-MS-based label-free quantitative proteomic profiling was performed.
- Building on the initial biomarker discovery analysis, an extended analysis was conducted by incorporating proteomic data from healthy controls and stratifying patients into high- (partial response and stable disease) and low- (progressive disease) response groups based on variable clinical response data. Principal component analysis was used to characterize patient-specific longitudinal changes in plasma proteomic profiles.
- Generative AI-based longitudinal modeling and candidate biomarker analysis were performed by SilicoPharm Inc. using its omics foundation model platform, KnockG™. Based on the observed longitudinal proteomic data, patient-specific proteomic trajectories were modeled through Cycle 12. Proteins showing distinct temporal abundance patterns between the high- and low-response groups were prioritized as candidate response-associated biomarkers and were further evaluated in the NSCLC-versus-healthy-control proteomic comparison.

Results

- Proteomic profiling identified 1,991 proteins in healthy controls and 2,041 proteins in patients with NSCLC, with 1,791 proteins commonly detected in both groups (**Figure 1**).

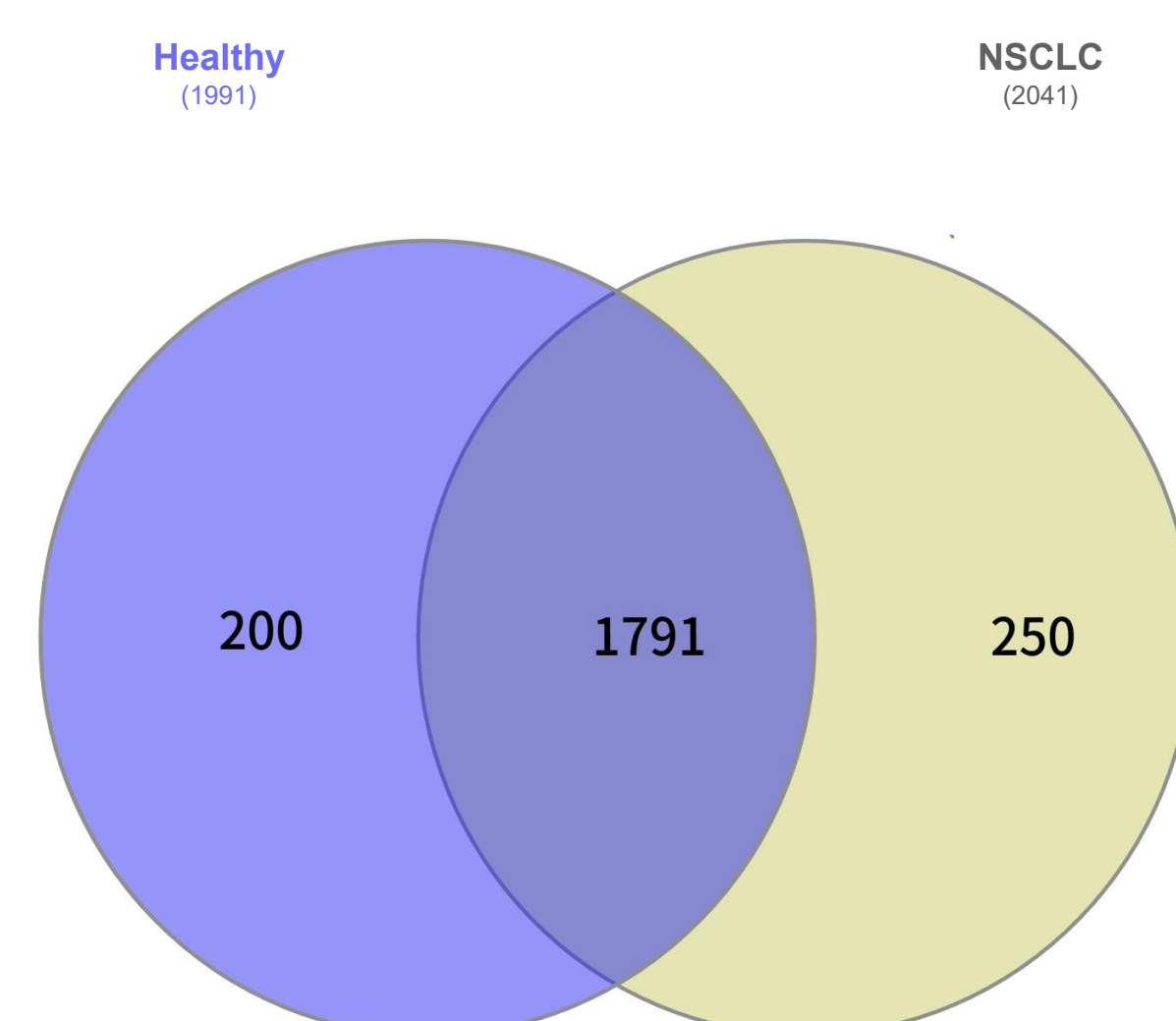


Figure 1. Plasma proteomic landscape in healthy controls and patients with NSCLC

- Longitudinal principal component analysis and generative AI-based modeling demonstrated patient-specific changes in plasma proteomic profiles during JIN-A02 treatment and enabled modeling of individual proteomic trajectories through Cycle 12 (**Figure 2**).

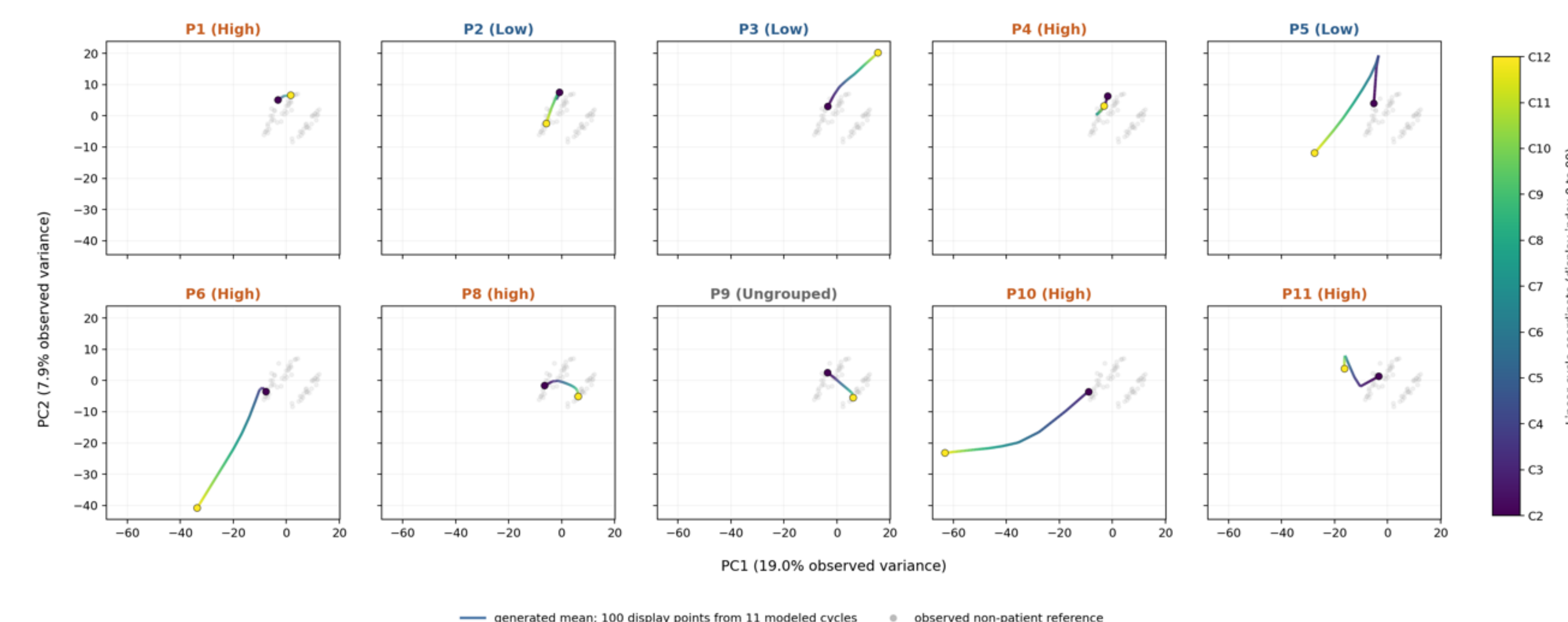


Figure 2. Longitudinal plasma proteomic trajectories during JIN-A02 treatment

- Comparison of the high- and low-response groups identified a subset of proteins exhibiting distinct longitudinal abundance patterns (**Figure 3**). Among these candidates, TPM3 showed an early positive trajectory in the high-response group and a higher modeled abundance over the treatment course compared with the low-response group.

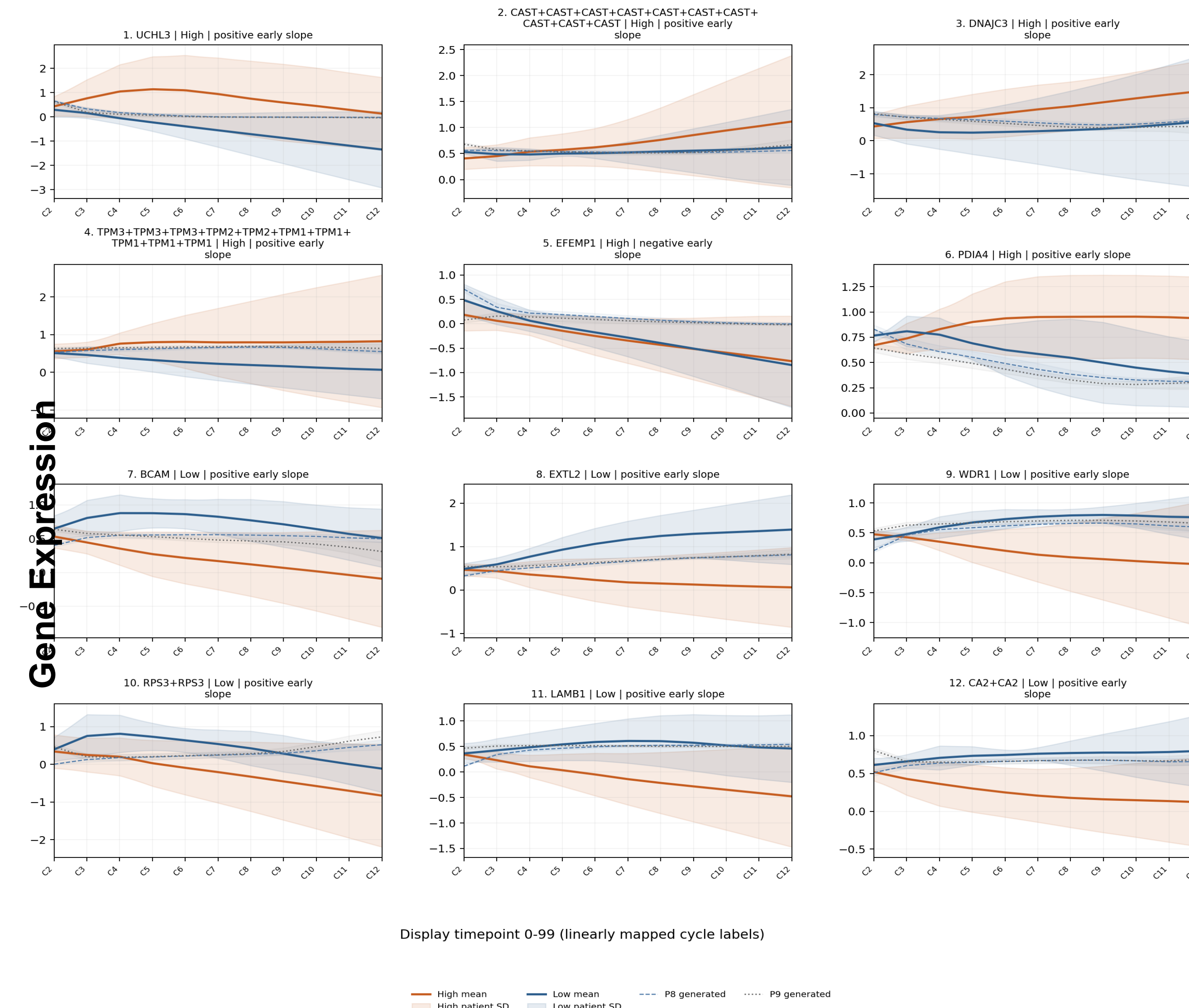


Figure 3. Identification of candidate response-associated biomarkers in high- and low-response groups

- In the overall cross-sectional proteomic comparison, TPM3 abundance was also higher in patients with NSCLC than in healthy controls (**Figure 4**).
- These findings nominate TPM3 as an exploratory circulating biomarker candidate associated with a favorable response to JIN-A02.

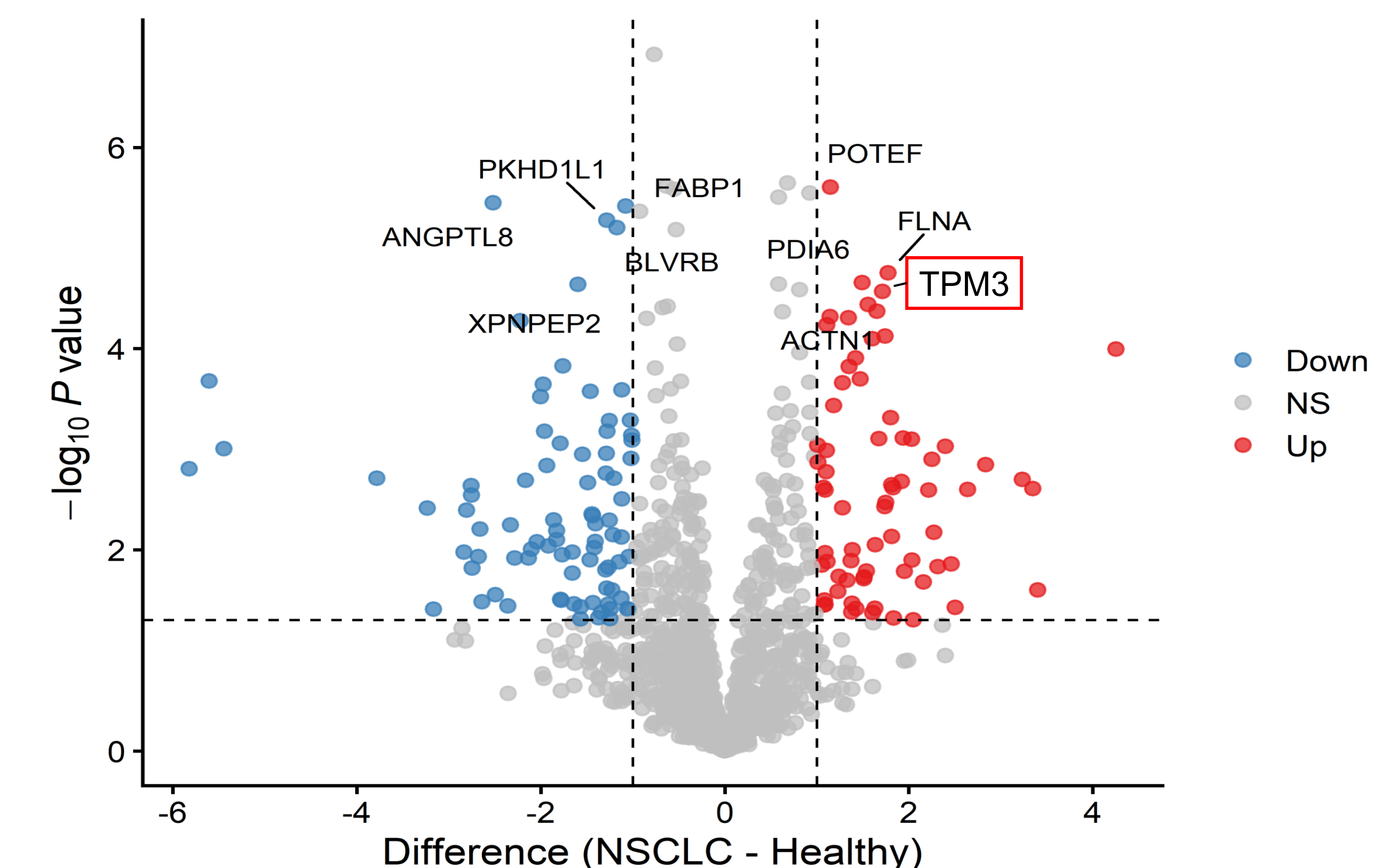


Figure 4. Increased TPM3 abundance in NSCLC patients compared with healthy controls

CONCLUSION

- The extended longitudinal analysis combining plasma proteomic profiling with generative AI-based modeling identified distinct proteomic trajectories associated with clinical response to JIN-A02. In particular, TPM3 exhibited a higher and more positive longitudinal abundance pattern in the high-response group, supporting its further evaluation as an exploratory response-associated biomarker.
- The observed longitudinal pattern suggests that circulating TPM3 may have potential for noninvasive response monitoring during JIN-A02 treatment. Its potential utility as a predictive patient-selection biomarker should be further evaluated by determining whether pre-treatment TPM3 levels can distinguish patients who subsequently derive greater clinical benefit from JIN-A02.

ACKNOWLEDGMENTS

- This research was also supported by the Scale-up TIPS Program, funded by the Ministry of SMEs and Startups (MSS), Republic of Korea 2420033037, RS-2026-25606940)
- This research was supported by Seoul R&BD Program (BT250189) through the Seoul Business Agency (SBA) funded by The Seoul Metropolitan Government
- This research was supported by Korea Drug Development Fund funded by Ministry of Science and ICT, Ministry of Trade, Industry, and Resources and Ministry of Health and Welfare (2710086652, RS-2025-02183074, Republic of Korea)