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Open-Data Serum Metabolomics of Lung Adenocarcinoma for Equitable Early Detection under SDG Target 3.4

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ABSTRACT

Objective: *Sustainable Development Goal (SDG) target 3.4 addresses premature non-communicable disease mortality, yet lung cancer leads cancer mortality among Indonesian men, and low-dose computed tomography screening presumes imaging capacity most low-income settings lack. This study asked which serum pathways are recoverable from open lung adenocarcinoma metabolomics and whether their enzymes are altered in tumor tissue.* ***Method:*** *Serum GC-TOF MS data from the ST000385 ADC2 cohort (43 cases, 43 controls, 152 compounds) were reanalysed in MetaboAnalyst 6.0 using PLS-DA with permutation testing, multivariate ROC, and KEGG enrichment. Enzymes were examined in TCGA-LUAD (483 tumor, 347 normal) with GEPIA2 and survival survival analysis, and the cohort ST000386 underwent metadata testing.* ***Results:*** *The one-component model separated the groups ($R^2 = 0.492$, $Q^2 = 0.302$, permutation $p < 5 \times 10^{-4}$) and reached an AUC of 0.882 on five metabolites, which a sensitivity analysis showed to rest on one correlated axis. Twenty metabolites passed a 5% FDR, and arginine biosynthesis was the most enriched pathway (FDR = 5.8×10^{-5}), whereas the TCA cycle and taurine metabolism did not survive correction. LDHA, PKM and CDO1 predicted survival. ARG1, OTC and CPS1 medians fell in tumor while ASS1 and ARG2 rose modestly. ST000386 carried subject-level metadata that does not associate with its own metabolome.* ***Novelty:*** *The dominant pathway is arginine biosynthesis rather than the Warburg axis of earlier readings, and the enzyme layer shows a dysregulated rather than silenced urea cycle.*

INTRODUCTION

Sustainable Development Goal (SDG) target 3.4 commits member states to cutting premature mortality from non-communicable diseases by one third by 2030, and cancer is the component of indicator 3.4.1 making the least progress (Cancela et al., 2023; Frieden et al., 2020; Liu et al., 2021). Lung cancer dominates that shortfall, with 2.48 million new cases and 1.8 million deaths estimated for 2022 (Zhou et al., 2024), and it is the leading cause of cancer death among Indonesian men, while the regional burden concentrates rather than eases (Asmara et al., 2023; Dee et al., 2025). Lung Adenocarcinoma (LUAD) is the commonest subtype of Non-Small Cell Lung Cancer (NSCLC) and is heterogeneous in driver mutation and metabolic phenotype (Herbst et al., 2018; Travis et al., 2015). The gap to the SDG trajectory largely stems from late-stage diagnosis, since stage III or IV presentation drives excess mortality in low- and middle-income settings (Hanafi et al., 2024; Henke et al., 2023). Low-Dose Computed Tomography (LDCT) screening lowers lung cancer mortality by approximately 20% in heavy smokers (National Lung Screening Trial Research Team, 2011) but flags most benign findings as positive (Mazzone et al., 2021) and presumes imaging capacity that cannot be assumed where the burden grows fastest, whereas no blood-based marker yet refines risk well enough to deploy (Seijo et al., 2019).