[BIOINFO 2025]

Plasma Cell-free Transcriptome Enables Early Detection and Stage-Stratification of Aggressive Solid Tumors

Jimin Seo[1], Na Young Kwon[1], Ki Wook Lee[1], Hyun Woo Park[1], Hye Jung Min[1], Heeje Cho[1],

Minho Choi[1], Yeju Kim[1] and Young-Jun Jeon[1,*]

[1]*Department of Integrative Biotechnology, Sungkyunkwan University*
**Corresponding author: jeon2020@skku.edu*

The plasma cell-free transcriptome (cfRNA) is a promising biomarker that can overcome the limitations of conventional diagnostic methods by enabling disease detection and monitoring at the transcriptome level. Using our home-made sequencing platform, LUNA-seq, we analyzed cfRNA from patients with aggressive solid tumors across both early and advanced clinical stages, together with cfRNA from healthy controls, to evaluate the potential for early detection. We identified 71 candidate gene sets that achieved an AUC > 0.9 in both discovery and test cohorts, and through optimization derived a final 39-gene set signature. This signature effectively distinguished early-stage patients from healthy individuals and showed a significant stepwise increase with advancing clinical stage. In survival analysis, higher signature scores were associated with a tendency toward reduced disease-free survival (DFS) and showed a similar trend in overall survival (OS). Importantly, external validation using independent cfRNA datasets confirmed that the signature not only discriminated healthy individuals but also significantly distinguished pre-cancerous states and other cancer types. These findings demonstrate the strong potential of cfRNA profiling with LUNA-seq for clinically applicable early detection and stage-stratification of aggressive solid tumors, as well as its broader utility in cancer diagnostics.