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Evaluating Plasma Cell-Free mRNA as a Biomarker for Early Detection of Aggressive Solid Tumors

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Liquid biopsy provides a non-invasive and practical approach for routine monitoring, reducing patient discomfort during diagnosis while facilitating precision medicine, in contrast to traditional tissue biopsies. Cell-free mRNA (cf-mRNA) has garnered significant attention in liquid biopsy research, with emerging studies supporting its potential as a biomarker. In this study, we assessed the ability of plasma cf-mRNA to identify cancer signatures, including in early-stage cases, among patients with aggressive solid tumors. Utilizing a novel cf-mRNA analysis platform, we investigated advanced-stage cancer patients (AJCC IIB+III, N=22), early-stage patients (AJCC I+IIA, N=12), and healthy controls (N=8). By computing enrichment scores for predefined gene sets that are highly expressed in early-stage solid tumors, we identified 29 gene sets exhibiting robust classification performance (AUC > 0.9) between advanced-stage cancer patients and controls. Additionally, 13 of these gene sets showed strong classification potential (AUC > 0.8) in early-stage cancers, and three gene sets maintained similar performance (AUC > 0.8) when validated using external RNA-seq tissue data. These results demonstrate the potential of cf-mRNA for the early detection of aggressive solid tumors, with further large cohort studies needed to explore its clinical applicability.