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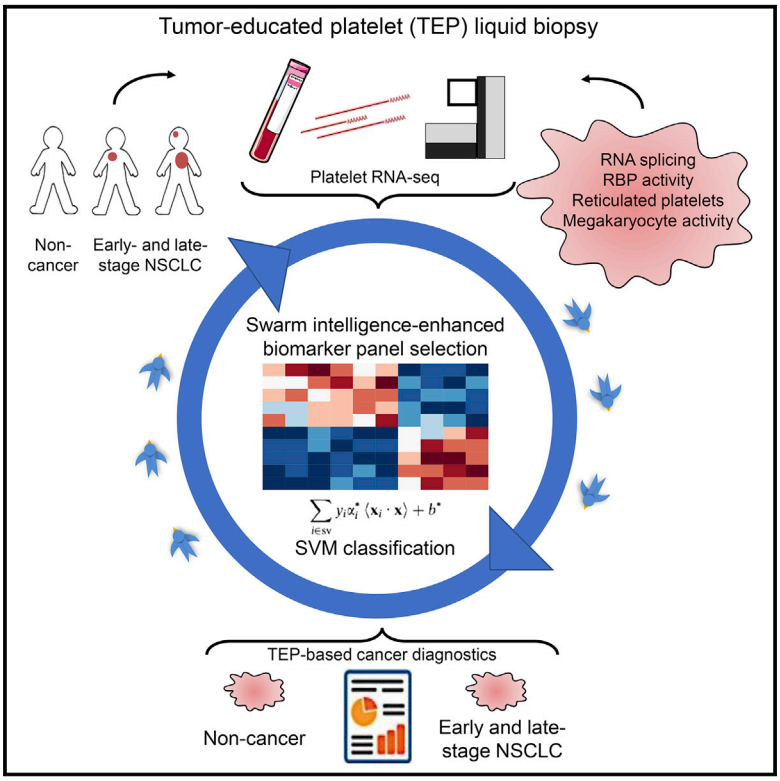
Swarm Intelligence-Enhanced Detection of Non-Small-Cell Lung Cancer Using Tumor-Educated Platelets

Graphical Abstract



Highlights

- Tumor-educated platelet (TEP) RNA profiles allow for blood-based cancer diagnostics
- Inflammatory conditions only minimally confound TEP-based cancer detection
- Swarm intelligence algorithms enable efficient selection of biomarker gene panels
- TEP gene panels enable support vector machine-based classification of lung cancer

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In Brief

Best et al. use particle-swarm optimization algorithms and RNA-seq of tumor-educated platelets from patients to generate RNA sets capable of identifying patients with non-small-cell lung cancer, including those having early stage, from individuals without cancer, including those having inflammatory conditions.

Data Resources

GSE89843

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Swarm Intelligence-Enhanced Detection of Non-Small-Cell Lung Cancer Using Tumor-Educated Platelets

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SUMMARY

Blood-based liquid biopsies, including tumor-educated blood platelets (TEPs), have emerged as promising biomarker sources for non-invasive detection of cancer. Here we demonstrate that particle-swarm optimization (PSO)-enhanced algorithms enable efficient selection of RNA biomarker panels from platelet RNA-sequencing libraries (n = 779). This resulted in accurate TEP-based detection of early- and late-stage non-small-cell lung cancer (n = 518 late-stage validation cohort, accuracy, 88%; AUC, 0.94; 95% CI, 0.92–0.96; p < 0.001; n = 106 early-stage validation cohort, accuracy, 81%; AUC, 0.89; 95% CI, 0.83–0.95; p < 0.001), independent of age of the individuals, smoking habits, whole-blood storage time, and various inflammatory conditions. PSO enabled selection of gene panels to diagnose cancer from TEPs, suggesting that swarm intelligence may also benefit the optimization of diagnostics readout of other liquid biopsy biosources.

INTRODUCTION

Non-invasive collection of cancer-associated circulating biomarkers enables efficient, rapid, and detailed molecular characterization of tumors. Recent advancements in isolation and characterization of cell-free DNA, plasma RNA, circulating proteins, circulating tumor cells, extracellular vesicles, and tumor-educated platelet (TEP) RNA facilitated detection of cancer-specific genomic and transcriptomic aberrations in blood (Alix-Panabières and Pantel, 2016; Best et al., 2015; Bettegowda et al., 2014; Chan et al., 2013; Newman et al., 2016; Nilsson et al., 2011, 2015; Skog et al., 2008; Wan et al., 2017). Blood platelets act as local and systemic responders during tumorigenesis and cancer metastasis (McAllister and Weinberg, 2014), thereby being exposed to tumor-mediated platelet education, and resulting in altered platelet behavior (Kerr et al., 2013; Labelle et al., 2011; Schumacher et al., 2013). We have previously demonstrated that TEP RNA can function as a biomarker trove to detect and classify cancer from blood via self-learning support vector machine (SVM)-based algorithms (Best et al., 2015). We

Significance

Detection of cancer in a minimally invasive manner is considered the holy grail for cancer diagnostics. A notorious challenge is the identification of optimal biomarker panels from such liquid biosources. To select robust biomarker panels for disease classification the use of "swarm intelligence" was proposed, especially particle-swarm optimization (PSO). PSO-driven algorithms are inspired by the concomitant swarm of birds and schools of fish that by self-organization efficiently adapt to their environment. Here, PSO algorithms are exploited for the identification of optimal biomarker gene lists, resulting in a tumor-educated platelet RNA biomarker panel that discriminates patients with NSCLC from healthy individuals and patients with various non-cancerous inflammatory conditions. Follow-up analysis of additional early-stage cancer patients is warranted.

