

Spectroscopic Profiling of Extracellular Vesicles as Emerging Biomarkers for Sepsis-Associated ICU-Acquired Weakness

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Raman Spectroscopy (RS) and Fourier-Transform Infrared (FT-IR) spectroscopy are powerful, label-free techniques with a clinical potential for the discovery of new biomarkers¹.

Here, we applied these complementary **vibrational spectroscopies** to address the major unmet clinical need related to the lack of specific biomarkers for early diagnosis of sepsis-associated Intensive Care Unit–Acquired Weakness (ICU AW+S)², using **Extracellular Vesicles** (EVs).

EVs are natural nanoparticles released by all cell types, emerging as promising biomarkers for non-invasive disease diagnostics in different pathologies. Indeed, EVs transport bioactive molecules that mirror the parental cells playing a key role in intercellular communication³.

RS and FT-IR analysis of EVs from healthy controls (HC), sepsis patients, and ICU AW+S patients revealed disease-specific spectral signatures. In particular, RS was predominantly sensitive to changes in the lipids' region, indicating probably dysregulation in lipid metabolism. In contrast, FT-IR spectroscopy highlighted differences mainly in protein and nucleic acid regions, suggesting stress or damage biochemical alterations.

Furthermore, multivariate analysis provided an integrated interpretation of the spectroscopic data, reinforcing these observations. Indeed, PCA–LDA of EV Raman spectra was able to discriminate among ICU AW+S, sepsis, and HC groups with an accuracy of 83.5%, while PCA of EV FT-IR data revealed group-specific trajectories.

Overall, the integrated RS and FT-IR EV analysis provides a biochemical fingerprint of ICU AW+S, supporting their potential as label-free tools for early **diagnosis** and bedside management of patients.

References

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