Seminar in Medical Microbiology

Title: Advancing SERS-Based Liquid Biopsy: From Substrate Engineering to Clinical Differential Diagnosis

Student: Mr. Patipan Wongboothong **ID:** 677070005-9

Advisor: Prof. Dr. Kiatichai Faksri

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Abstract

Surface-Enhanced Raman Scattering (SERS) has emerged as a powerful optical approach for non-invasive biomedical diagnostics, promising great sensitivity and accuracy for molecular fingerprinting utilizing biofluids. By leveraging localized surface plasmon resonances (LSPR) in noble metal nanostructures, SERS amplifies weak Raman scattering signals from biomolecules, enabling the detection of subtle biochemical changes associated with pathological conditions. Despite its potential, clinical adoption of SERS is constrained by challenges, including substrate stability, signal reproducibility, and the difficulty of distinguishing diseases with overlapping pathogeneses.

Recent studies present distinct strategies to address these diagnostic challenges. To improve spectral reproducibility, Lu et al., (2023) fabricated a stable solid-state Gold Nanocone Array (Au NCA) substrate using polystyrene colloidal sphere template-assisted reactive ion etching and magnetron sputtering. Their findings indicated that a 50-fold serum dilution minimized viscosity interference while preserving signal intensity, enabling reliable differentiation between gastric cancer patients and healthy controls with high spectral stability. Conversely, Khristoforova et al., (2025) investigated the clinical application of SERS with silver (Ag) colloids to distinguish complex respiratory conditions. Their study employed Partial Least Squares Discriminant Analysis (PLS-DA) to separate Chronic Obstructive Pulmonary Disease (COPD) and Bronchial Asthma (BA) from Chronic Heart Failure (CHF). Although the model achieved high accuracy (0.92) to differentiate respiratory diseases from CHF using markers such as uric acid and glycogen, differentiation between COPD and BA remained challenging, suggesting shared metabolic pathways between these conditions.

In conclusion, this seminar highlights the progress of SERS for clinical use. However, distinguishing diseases that share the same metabolic pathways remains a challenge, indicating a need for improved spectral data analysis and the widespread adoption of standardized substrates. Ongoing technological advancements are expected to enhance the efficacy of SERS as a diagnostic tool.

Reference

Khristoforova, Y., Bratchenko, L., Kupaev, V., Senyushkin, D., Skuratova, M., Wang, S., Lebedev, P., & Bratchenko, I. (2025). Detection of Respiratory Disease Based on Surface-Enhanced Raman Scattering and Multivariate Analysis of Human Serum. *Diagnostics*, *15*(6), 660. https://doi.org/10.3390/diagnostics15060660

Lu, Y., Lei, B., Zhao, Q., Yang, X., Wei, Y., Xiao, T., Zhu, S., Ouyang, Y., Zhang, H., & Cai, W. (2023). Solid-State Au Nanocone Arrays Substrate for Reliable SERS Profiling of Serum for Disease Diagnosis. *ACS Omega*, *8*(32), 29836–29846. https://doi.org/10.1021/acsomega.3c04910