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# Fluorescence-Raman (Dual-modal) Endoscopic System for Real-time *in vivo* Multiplexed Molecular Diagnosis

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## 1. Introduction

Optical-based endoscopic imaging techniques have been intensively explored for use in the diagnosis of specific cancers involving gastric, lung, colon, and bladder cancer due to its accessibility to internal organs and real-time imaging with minimally invasive procedure. [1] However, subtle neoplastic changes are difficult to identify using solely conventional white light reflectance (WLR) endoscopy in flat and suspicious lesions because it can only distinguish visually observable morphological changes. For this reason, to improve the accuracy of endoscopic diagnosis in early stage of specific cancer, additional functionalities have been combined with endoscopic system such as fluorescence, bioluminescence, and Raman scattering. [2-3]

## 2. Result and Discussion

In this study, we developed the real-time fluorescence-Raman (dual-modal) endoscopic system (FRES) for *in vivo* multiplexed molecular diagnosis incorporating fluorescence-SERS active nanoprobe (F-SERS dots), which can simultaneously emit fluorescence and Raman signal, as tumor targeting agents. The FRES were designed to simultaneously detect fluorescence and Raman signal that allowed real-time fluorescence images to track the targeted location and Raman spectra to identify the targeted probe. The simultaneous dual signal detecting ability of FRES was evaluated by detecting very low concentrations of F-SERS dots (down to 1-pM corresponding to 325 F-SERS dots) which can meet the sensitivity standard to be used as a diagnostic tool. To demonstrate the usability and effectiveness of FRES for *in vivo* endoscopic molecular diagnostics, we performed multiplexed active targeting, real-time imaging, and identifying multiple biotargets (HER2 and EGFR) in breast cancer xenograft model. The HER2 and EGFR were specifically targeted by two kinds of antibody conjugated F-SERS dots and successfully identified based on the real-time fluorescence images and Raman spectra provided by FRES at the same time.

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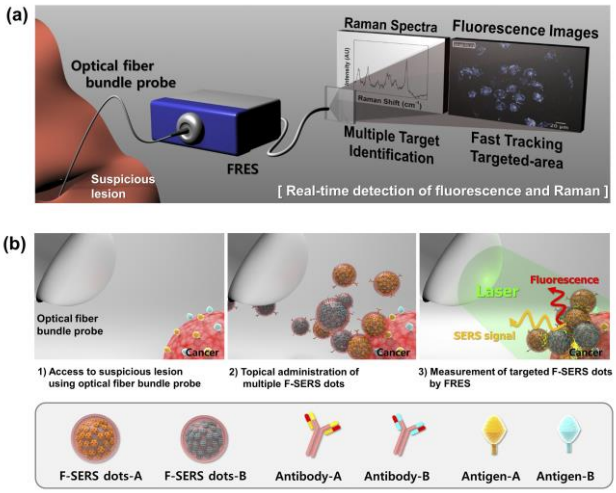


**Figure 1.** Schematic illustration of real-time multiplexed imaging using the fluorescence-Raman endoscopic system (FRES). (a) The mode of dual modal detection with fluorescence and Raman scattering. (b) Illustration of the *in vivo* multiplexed molecular imaging procedure.

## 3. Conclusions

We have developed a fluorescence-Raman endoscopic system (FRES) with fluorescence-SERS active nano-probes (F-SERS dots) and successfully demonstrated *in vivo* dual modal detection of multiple targets for specific cancer. The fluorescence images and Raman spectra were simultaneously obtained in real-time, and the multiple bio-targets in breast cancer model were easily tracked and clearly identified by FRES. Based on these result, we can believe that FRES has a significant potential as a clinical molecular diagnostic tool which can be utilized during routine endoscopic procedure.

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