Abstract Submission Form: ASEAN IVO Forum 2024

I. Title of presentation: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

II. Name and Institution: Khon Kaen University, Thailand

III. Abstract

Cholangiocarcinoma (CCA), a highly prevalent cancer in the Greater Mekong Subregion, particularly in northeastern Thailand and Lao PDR, is closely linked to infections from the liver fluke *Opisthorchis viverrini*. Unfortunately, most CCA cases are diagnosed at advanced stages, significantly limiting treatment options and resulting in poor post-surgical survival rates. One of the key challenges in CCA management is the lack of reliable and easily accessible biomarkers for early diagnosis. Current diagnostic methods, such as radiological imaging and histopathological examination, are both expensive and time-consuming.

To address this issue, our research has focused on identifying biomarkers for CCA in animal models, with promising potential for translation into clinical applications. The next phase of the project aims to develop and implement biosensor platforms utilizing advanced photonic and electrochemical detection technologies. These platforms offer high integration capabilities, allowing for rapid and sensitive detection of trace biomarker levels across various biological samples, including urine, feces, and serum. Our objective is to transition these biosensor platforms from research labs to large-scale clinical applications, creating an accessible, cost-effective diagnostic tool for CCA.

By applying biomarkers identified in animal models to human diagnostics, we aim to establish a reliable system for early-stage CCA detection, thereby improving patient survival rates through timely intervention. Future connected projects will focus on refining these biosensor technologies and expanding their use in clinical medicine and analytical chemistry for the diagnosis of other diseases. The project integrates various optical and electrochemical sensing technologies for CCA diagnosis. To achieve this goal, we have established collaborations with several institutions, including the Faculty of Medicine at Khon Kaen University (MD-KKU), the Department of Computer Engineering at KKU (EN-KKU), Chiang Mai University's Faculty of Engineering (CMU), Thai Microelectronics Center (TMEC), The National Center for Genetic Engineering and Biotechnology (BIOTEC), The National Electronics and Computer Technology Center (NECTEC), and Japan's NICT. We also work closely with the Cancer Center in Lao PDR (National Institute in Laos), with networking support from NICT to facilitate Thai-Lao collaborations.

The project is structured into four work packages (WPs): **WP1**: Development of a biosensing platform based on Raman spectroscopy. **WP2**: Development of a biosensing platform based on silicon photonic sensing technology. **WP3**: Application of these biosensing platforms in clinical settings. **WP4**: Project management and logistics.

MD-KKU has induced CCA at various stages in animal models using a combination of liver fluke infection and carcinogens. Various samples, including liver, blood, feces, and urine, were collected to identify candidate biomarkers using Raman spectroscopy. By employing surface-enhanced Raman spectroscopy (SERS) coupled with machine learning, we successfully distinguished different stages of CCA development, such as inflammation, precancerous lesions, and tumor formation, based on histopathological features. This aspect of the project was closely developed in collaboration with NECTEC and EN-KKU. Proteomic analysis, conducted with BIOTEC, identified several protein markers for CCA diagnosis. In parallel, biosensing platforms based on two different techniques were developed by the EN-KKU and CMU teams with support from NICT. EN-KKU applied Raman spectroscopy to identify CCA-specific fingerprints in lab-scale studies, leading to the development of a SERS chip for CCA diagnosis. Simultaneously, CMU used silicon photonic resonator devices to detect multiple protein markers for CCA. MD-KKU collaborated with both teams to design and test these biosensing platforms.

In addition, the Lao team established a cancer registry and organized sample collection efforts for CCA diagnosis in Lao PDR. The R&D outcomes of the project include the development of colloidal SERS, software licensing, and the design, fabrication, and implementation of photonic sensor devices for CCA diagnosis. Several candidate protein markers, such as Olf4, SMC2, B4GALT4, and betaHCG, were discovered in animal models and hold potential for use in human diagnostics.

The project's scientific contributions have been submitted for publication in international journals (currently under review) and were presented at the 83rd Annual Meeting of the Japanese Cancer Association (JCA 2024). In terms of societal impact, the successful development of the electrochemical and silicon photonic sensors will be applied for CCA diagnosis in Lao PDR. These biosensor platforms would be used for point-of-care CCA diagnosis in the region in the future, contributing to improved early detection and treatment outcomes.