Abstract Submission Form: ASEAN IVO Forum 2025

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

II. Name and Institution: Prof.Somchai Pinlaor, Khon Kaen University, Thailand

III. Abstract

1. Purpose and Background

Cholangiocarcinoma (CCA) represents a major public health crisis in the Greater Mekong Subregion, particularly in northeastern Thailand and Laos PDR, where infection with the human liver fluke, *Opisthorchis viverrini* (OV), is endemic. The high mortality rate of CCA is intrinsically linked to its late-stage presentation. Currently, diagnosis relies on radiology and histopathological confirmation, which are high-cost, time-consuming, and invasive. Consequently, patients are often diagnosed at an advanced stage when surgical intervention is ineffective, leading to poor survival outcomes. The critical unmet need is a biomarker for early detection. While several candidate biomarkers have been discovered in animal models, their translation to clinical application is hampered by the lack of sufficiently sensitive, rapid, and cost-effective detection platforms.

Recent advances in biosensor technology, specifically photonic and electrochemical detectors, offer a path forward. These platforms allow for a high degree of integration and sensitivity, making them ideal for detecting trace amounts of biomarkers in non-invasive samples like serum and urine. This project is built on the hypothesis that biosensing platforms used for biomarker discovery in animal models can be successfully translated into clinical tools for patient diagnosis. This proposal outlines an ASEAN IVO project, building on a 2019 MOU between MD-KKU and NICT, Japan. By uniting a network of experts from Thailand, Laos, and Japan, we aim to leverage cutting-edge technology to create a tangible solution for the CCA epidemic in the region.

2. Project Objectives and Overview

The primary objective of this project is to develop and validate innovative optical and electrochemical biosensing platforms for the early diagnosis of cholangiocarcinoma.

To achieve this, the project is structured into four main Work Packages (WPs) (see Figure 1) that create a synergistic workflow from discovery to clinical implementation:

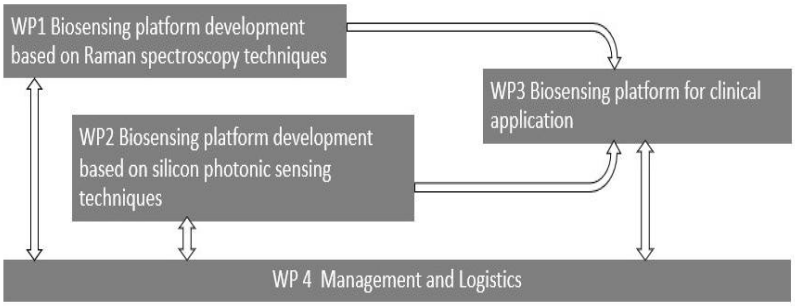

Figure 1 Workspace of project management.

WP1: Biosensing Platform Development (Raman Spectroscopy): To develop a Surface-Enhanced

Raman Spectroscopy (SERS) based platform and identify a unique "fingerprint" for CCA from animal model samples.

WP2: Biosensing Platform Development (Silicon Photonics): To develop a silicon photonic-based biosensor capable of detecting CCA protein markers simultaneously from a single sample.

WP3: Biosensing Platform for Clinical Application: To validate both biosensor prototypes using clinical samples from CCA patients in Thailand and to transfer this technology for implementation and validation in Lao PDR.

WP4: Management and Logistics: To ensure effective coordination, communication, and resource management across the multi-institutional and multinational project team.

3. Content: Methods and Implementation Plan

3.1 Work Package 1: Biosensing Platform Development (Raman Spectroscopy)

Principal Investigators: EN-KKU (Srichan & Danvirutai), MD-KKU (Prof. Pinlaor & team)

Participants: CMU, NICT

Timeline: April 2023 – Dec 2023

Activity 1.1: MD-KKU will establish animal models for various cholangiocarcinoma (CCA) stages (benign, early, advanced) and collect biological samples. Concurrently, EN-KKU will fabricate novel SERS chips using materials like 3D graphene or silver nanostructures, creating "hotspots" to amplify signals. Using these chips, the teams will analyze the samples to identify a unique Raman spectral "fingerprint" that can distinguish healthy controls from different CCA stages.

Activity 1.2: Raman Spectrometer Development Based on the specific, significant Raman wavenumbers identified in Activity 1.1, the team will design and build a CCA detector. This device will be miniaturized and customized to filter and detect only the wavelengths relevant to the CCA fingerprint, making it a specialized, cost-effective diagnostic tool.

Target (WP1): A SERS-based sensing device for early CCA diagnosis, developed from animal-based discovery and ready for clinical verification.

3.2 Work Package 2: Biosensing Platform Development (Silicon Photonics)

Principal Investigator: CMU (Mankong, Udomsom)

Participants: TMEC, MD-KKU, NICT

Timeline: Dec 2023 – April 2024

Activity 2.1: Sensor Design and Fabrication Building on previous successful collaborations that demonstrated single-biomarker detection, the CMU team will design and simulate advanced silicon photonic resonator devices and specialized microfluidic channels. These will be engineered to simultaneously detect multiple CCA protein biomarkers. Device fabrication will be conducted by TMEC.

Activity 2.2: System Integration and Prototyping The photonic sensor will be integrated into a functional prototype. This includes device packaging, software development, and the application of DSP/AI techniques to accurately interpret optical signal changes caused by the presence of target biomarkers in human samples.

Target (WP2): A prototype silicon photonic biosensor capable of detecting multiple CCA biomarker proteins in human samples.

3.3 Work Package 3: Biosensing Platform for Clinical Application
Principal Investigators: MD-KKU (Prof. Pinlaor & team), Lao PDR (Dr. Champadeng & team)
Participants: EN-KKU, NECTEC, BIOTECH, CMU, TMEC, NICT
Timeline: May 2024 – March 2025
Activity 3.1: Clinical Validation in Thailand (May – Sep 2024). With human ethics approval, the MD-KKU team will collect urine, and blood samples from CCA patients (confirmed by histopathology) and healthy controls. Both the SERS (WP1) and silicon photonic (WP2) prototypes will be tested on these samples. The efficacy, sensitivity, and specificity of the biosensors will be evaluated against standard tumor markers (e.g., CA19-9, CEA, AFP) and other methods such as ELISA and Western Blotting.
Activity 3.2: Technology Transfer and Validation in Laos (Oct 2024 – Mar 2025). A core goal of this project is technology transfer. The Thai and NICT teams will train technicians and physicians in Lao PDR through workshops and short courses. The validated protocols and biosensor platforms will be implemented at the Lao PDR Cancer Center. A parallel clinical validation study will be conducted using samples from Lao CCA patients to confirm the platforms' efficacy in a different clinical setting. Regular meetings will be held to evaluate procedures and results.
Target (WP3): Full validation of both biosensor platforms in clinical settings in Thailand and successful transfer and implementation of the technology in Lao PDR.
4. Leveraged Resources and Participant Roles: The unique/established expertise of its partners:
MD-KKU (CARI): As a leader in CCA research, CARI provides critical infrastructure, including established animal models, a large-scale biobank, clinical data, histopathological units, and extensive community/hospital-based patient networks.
EN-KKU: Brings expertise in plasmonic/photonic biosensors, machine learning for signal interpretation, and electrochemical nanodeposition for colloidal SERS chip development.
CMU: Provides specialized experience in silicon photonics design, simulation, and optical testing, along with established sensor functionalization techniques.
TMEC: Offers its CMOS fabrication facility for low-cost, precise fabrication of the photonic devices and microfluidics.
NICT (Japan): Provides essential high-level experience in optical device design and fabrication, supporting both the Raman and photonic teams.
Lao PDR Team: Offers crucial access to a high-incidence CCA patient population for clinical validation and field implementation.
5. Broader Impact and Plans for Connected Projects
Technical: It will create two novel biosensing platforms for CCA diagnosis: a SERS-based device and a colloidal SERS based device, and silicon photonic sensor.
Social & Future: These platforms will enable rapid, low-cost, and sensitive screening, improving public health. This early detection will lead to better patient outcomes, reduced mortality, and higher quality of life. The project also involves technology transfer to Lao PDR, building local capacity and strengthening the Thai-Laos-NICT network. This research will serve as a foundation for future R&D, potentially leading to at-home monitoring systems.