



# Project Title: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis



Speaker:

**Prof. Somchai Pinlaor**

Institute :

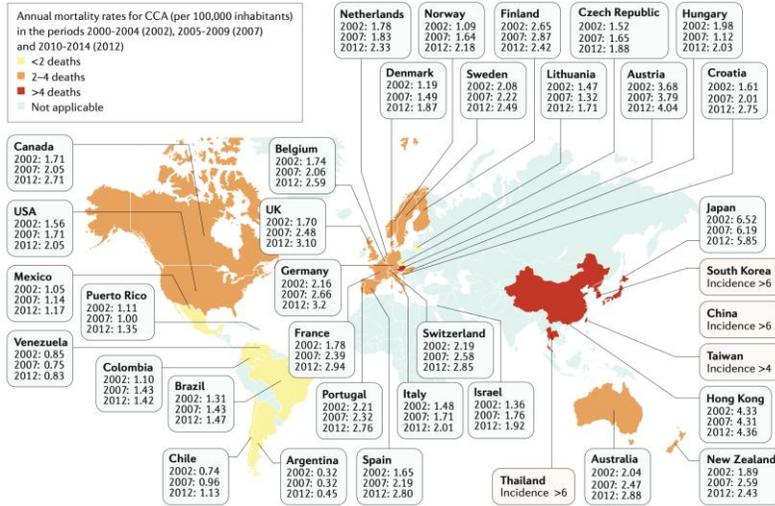
Khon Kaen University (KKU), Khon Kaen 40002, Thailand



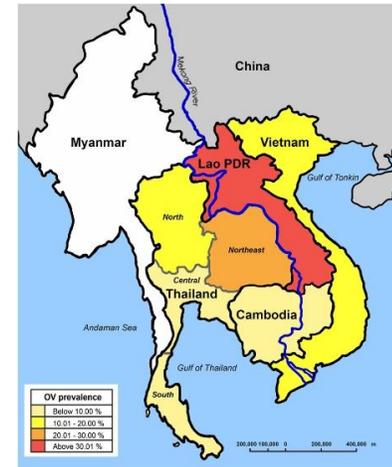
November 19, 2025; Singapore

# Project title: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

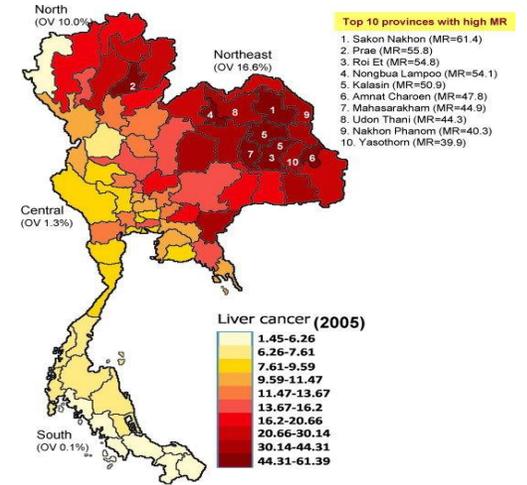
## Background



Banales. J.M. et al, 2020



Khuntikeo N et al. 2018



Sripa B et al. 2011

## Current diagnostic techniques

### Tumor screening



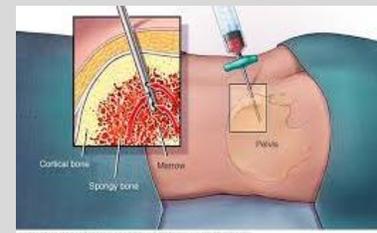
Ultrasound

### Confirmation

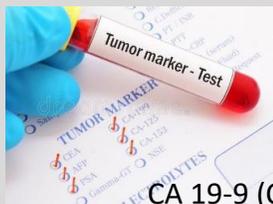


MRI

### Tumor type identifying & staging



Tissue biopsy



**Tumor markers: CA19-9, CEA, AFP**

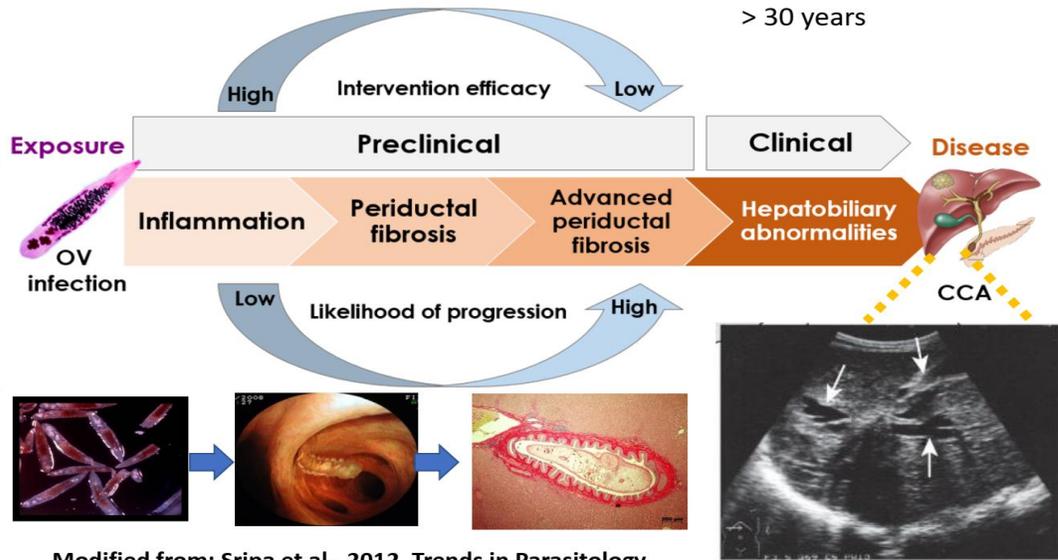
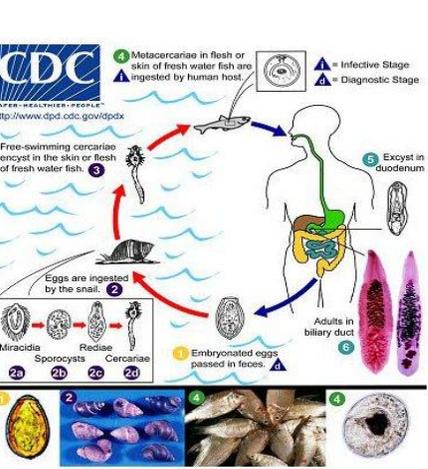
CA 19-9 (Carbohydrate Antigen 19-9), CEA (Carcinoembryonic Antigen), and AFP (Alpha-fetoprotein)

# Project title: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

## Background :

## Previous finding

*O. viverrini* infection contributes to CCA development



Modified from: Sripa et al., 2012, Trends in Parasitology

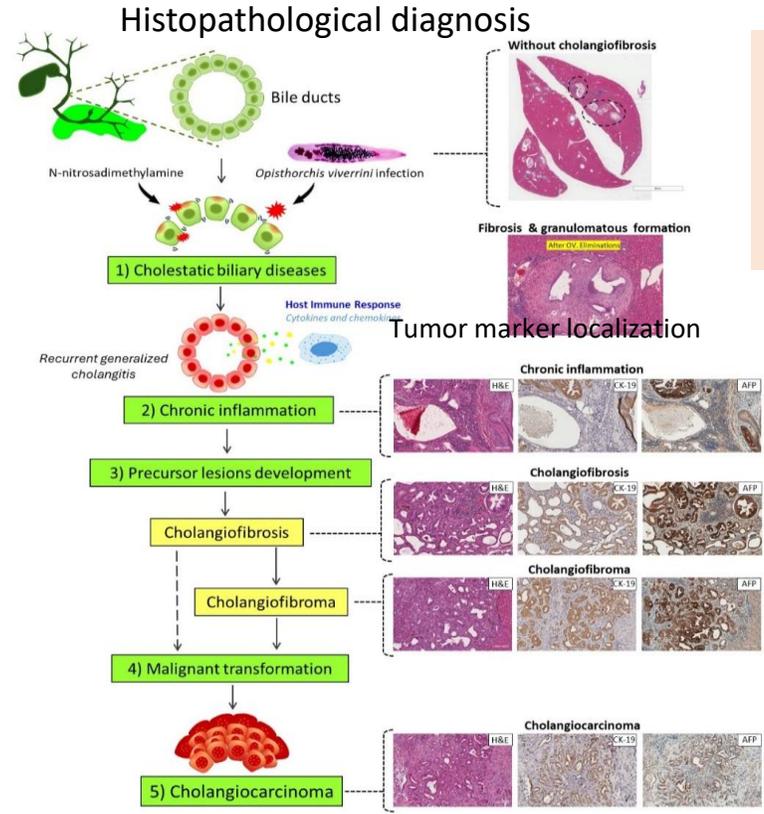
OV-induced inflammation, fibrosis, advanced fibrosis, and contribution risk to CCA. Thus, radiology such as MRI & Ultrasound are used for CCA screening.  
OV = *Opisthorchis viverrini*

## Target

To develop and validate innovative optical and electrochemical biosensing platforms for the early diagnosis of cholangiocarcinoma.

## Our hypothesis

CCA development is cell-type specific.



OV-induced chronic inflammation  
Precancerous lesion  
CCA lesions

# Project title: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

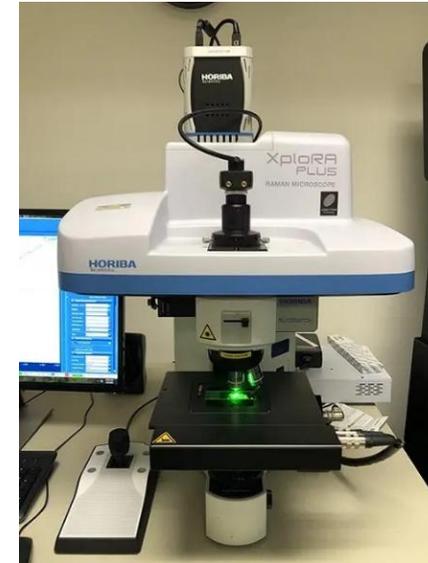
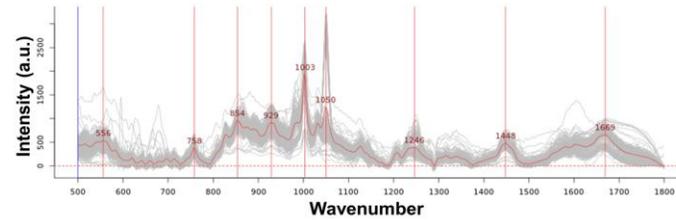
## Proposed methods

Biosensors and Bioelectronics 246 (2024) 115915  
 Contents lists available at ScienceDirect  
**Biosensors and Bioelectronics**  
 journal homepage: [www.elsevier.com/locate/bios](http://www.elsevier.com/locate/bios)

**Early-stage diagnosis of bladder cancer using surface-enhanced Raman spectroscopy combined with machine learning algorithms in a rat model**  
 Sanghwa Lee <sup>a,1</sup>, Miyeon Jue <sup>a,b,1</sup>, Kwanhee Lee <sup>c</sup>, Bjorn Paulson <sup>a,d</sup>, Jeongmin Oh <sup>e</sup>, Minju Cho <sup>e</sup>, Jun Ki Kim <sup>b,c,e,\*</sup>

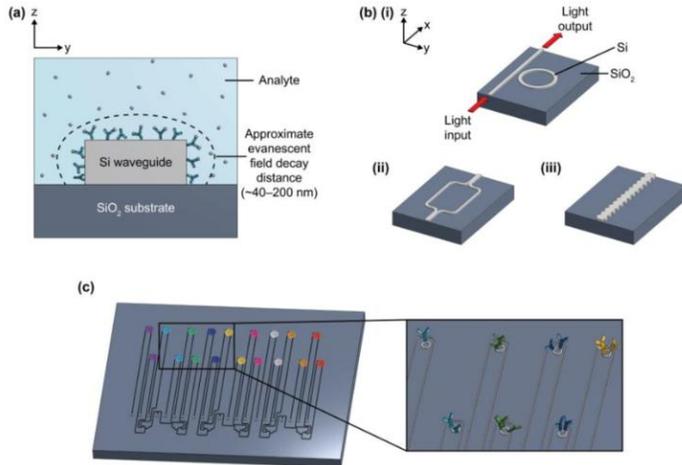
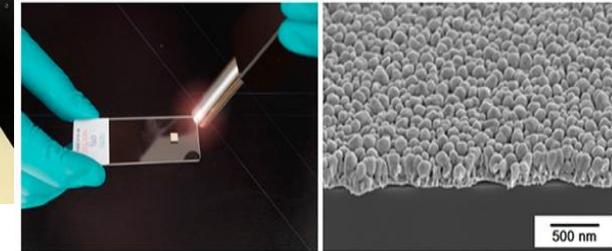
<sup>a</sup> Biomedical Engineering Research Center, Asian Institute for Life Sciences, Asian Medical Center, Seoul, 05505, Republic of Korea  
<sup>b</sup> Apollon, Inc., 68 Achaean-ro, Seongdong-gu, Seoul, 05505, Republic of Korea  
<sup>c</sup> Department of Biomedical Engineering, College of Medicine, University of Ulsan, Seoul, 05305, Republic of Korea  
<sup>d</sup> Morgridge Institute for Research, Madison, WI, 53715, USA

DNA, RNA, protein, peptide, lipid, etc.,



Raman spectroscopy

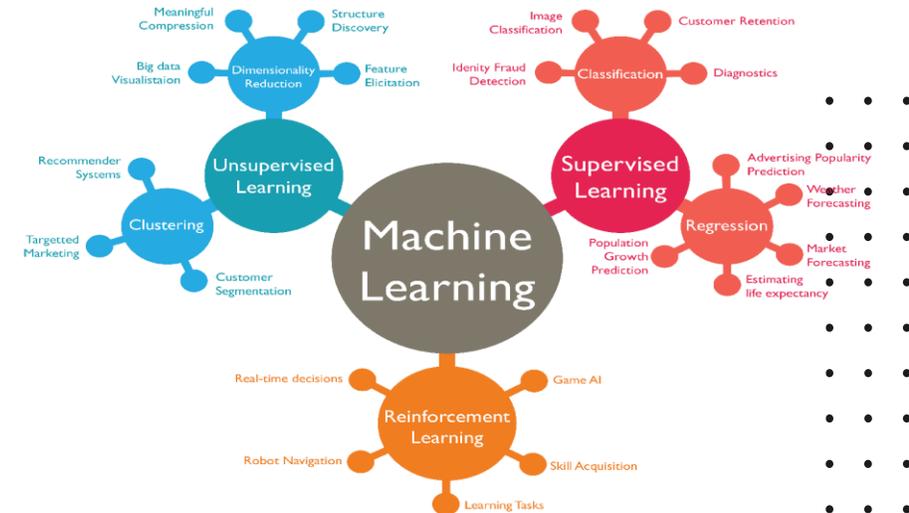
## NECTEC SERS Chips



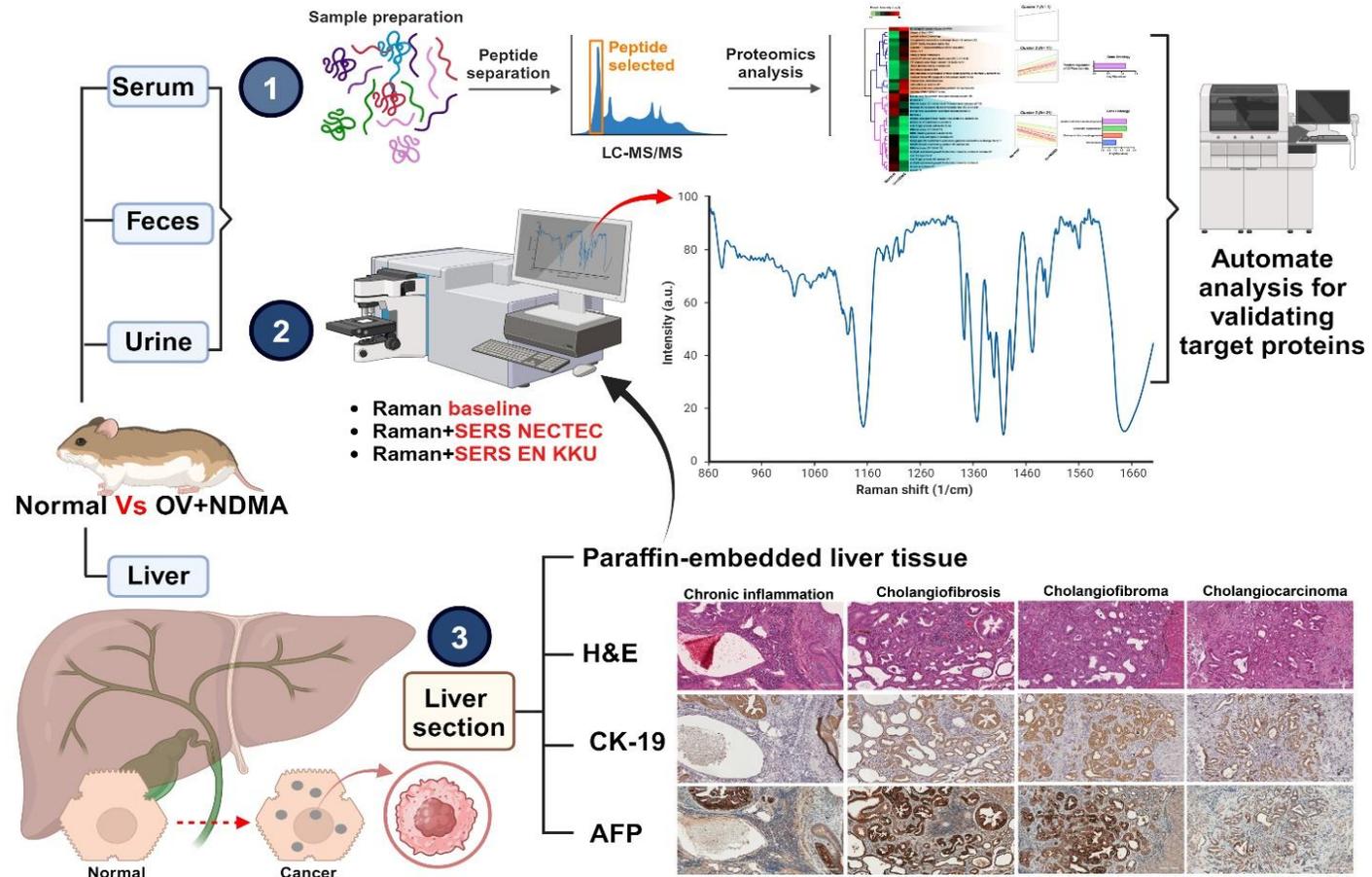
Silicon photonic sensor



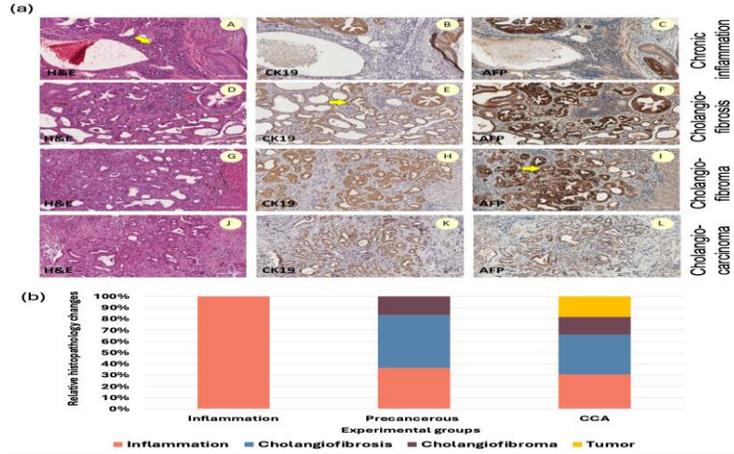
LC-MS/MS



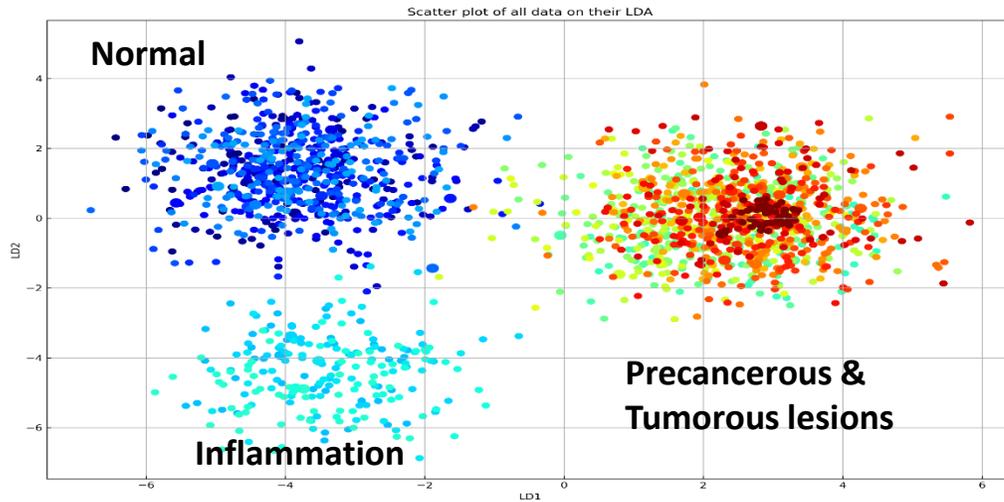
# Hamster's CCA establishment for hypothesis testing, proof-of-concept



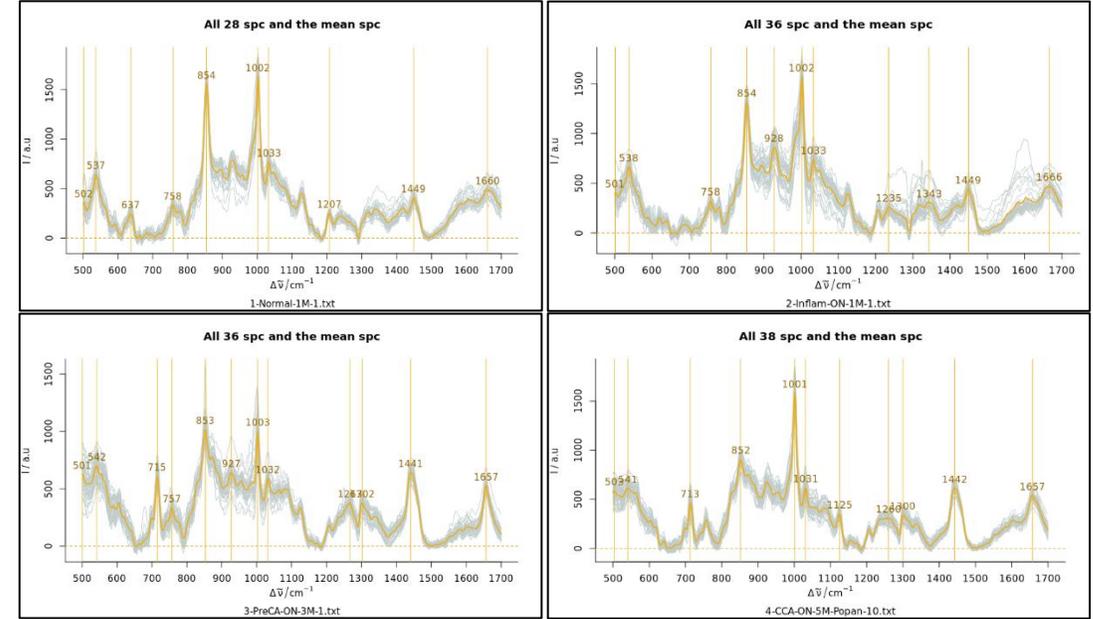
**Schematic diagram illustration of the scope of the study in animal model.** The step include 1) proteomic analysis for protein identification, 2) Raman spectroscopy based on based line peak, SERS from NECTEC and SERS from EN-KKU, and 3) histopathological study by staining with hematoxylin-eosin (H&E), cytokeratin-19 (CK-19) and alpha-fetoprotein (AFP).



CCA development is classified into inflammation, pre-cancerous lesion and tumor lesion according to histopathological changes



PCA was used to compare Raman spectra of four classes (Normal, Inflammation, Pre-cancer, Tumor). However, classical ML algorithms using Raman intensity could not distinguish between the Pre-cancerous and CCA (Tumor) groups.



Comparison among Raman peak based on classical machine (ML) algorithm of four classes based on normal, inflammation, pre-cancerous and tumor features.

	precision	recall	f1-score	support
Group 1-N	0.61	0.84	0.71	231
Group 2-I	0.40	0.07	0.11	61
Group 3-P	0.61	0.51	0.56	210
Group 4-C	0.65	0.65	0.65	220
accuracy			0.62	722
macro avg	0.57	0.52	0.51	722
weighted avg	0.61	0.62	0.60	722

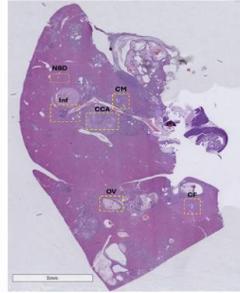
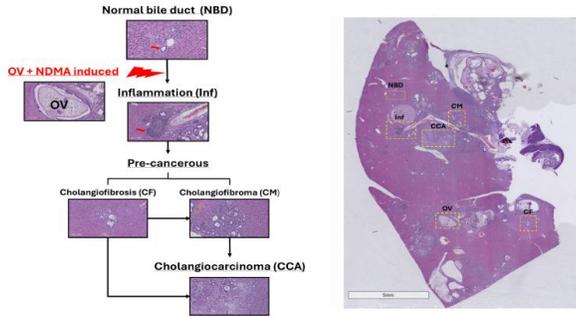
SERS couple with PCA couldn't distinguish precancerous-tumor lesion and yield accuracy of test 62%.

The integration of SERS and machine learning achieved a diagnostic sensitivity of 93%, specificity of 95%, and accuracy of  $\geq 67\%$  for precancerous lesions and CCA

# Project activities: MDKKU-ENKKU

## SERS + 2D CNN: A New Tool for Early CCA Diagnosis

## SERS + 2D CNN: A New Tool for Early CCA Diagnosis in animal



Different staging of CCA development was established.

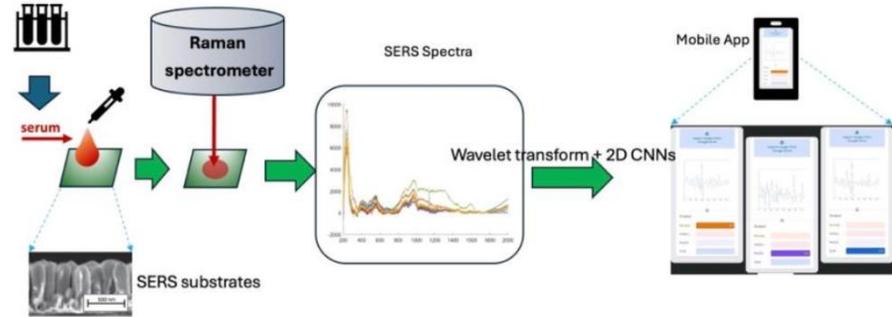
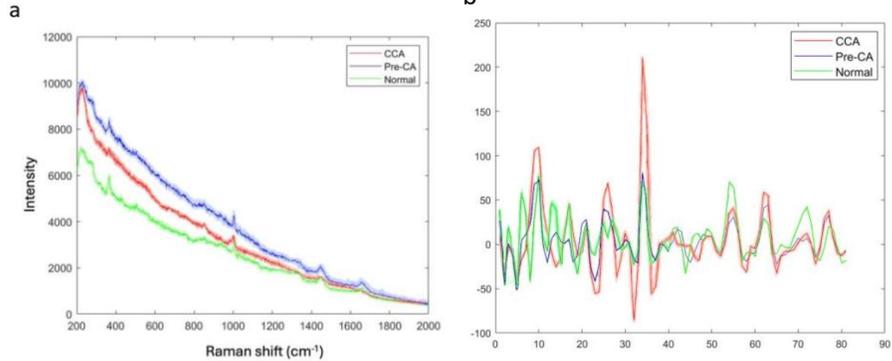
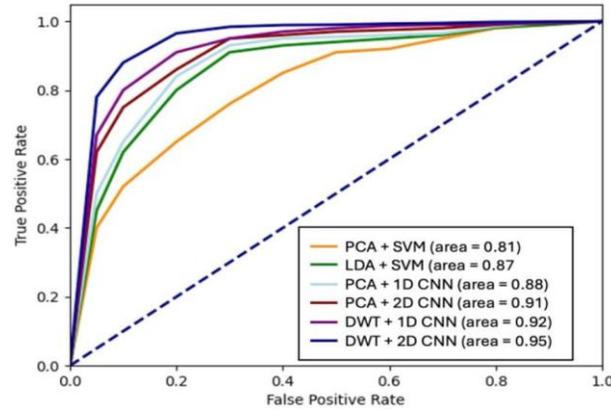


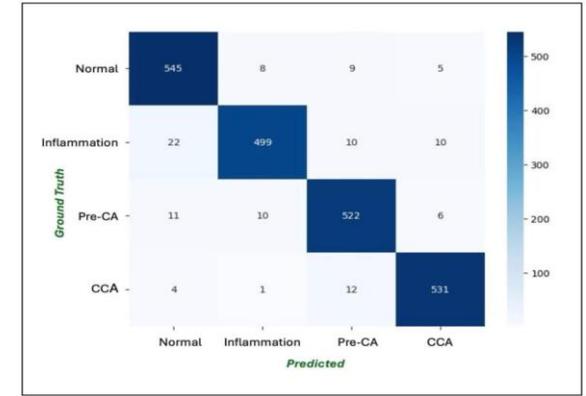
Illustration of study design for SERS+AI marks early stage of CCA



Raman peak identifies the different staging of inflammation, precancerous (Pre-CA) and CCA lesions



- ROC curve analysis was used to compare the performance of all classification models.
- The **DWT + 2D CNN** model demonstrated the highest accuracy for CCA diagnosis.
- **Result: AUC = 0.95**



Confusion matrices of each signal processing and machine learning methods by 2D CNN.

DWT = discrete wavelet transform

Method	Accuracy (%)	Sensitivity (Recall) (%)	Specificity (%)	F1 Score (%)
DWT + 2D CNN	95.10	95.08	98.36	95.10
DWT + 1D CNN	92.00	91.50	96.00	91.75
PCA + 1D CNN	88.00	87.50	94.00	87.75
LDA + SVM	84.50	84.00	90.50	84.25
PCA + SVM	82.40	82.00	88.40	82.20

**Accuracy 95%, sensitivity 95%. Specificity 96%**

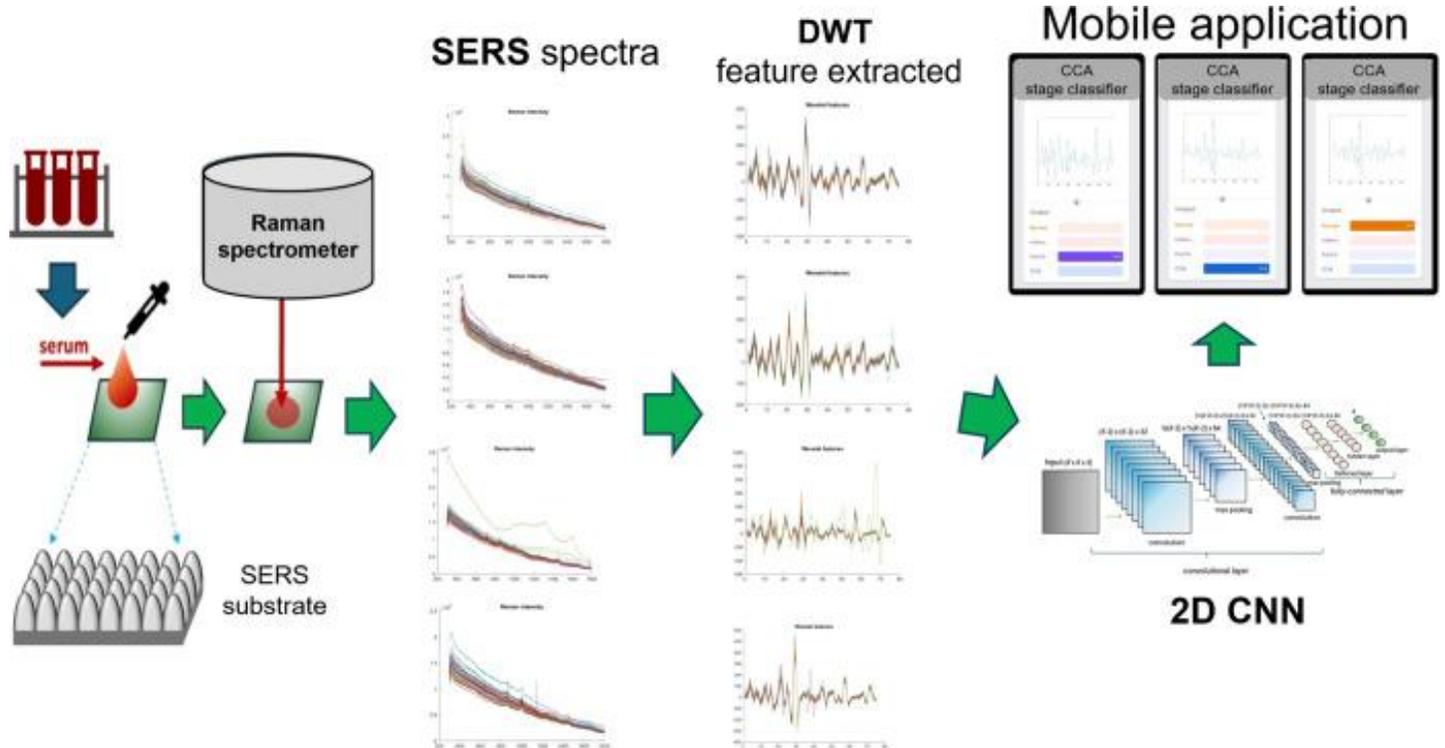
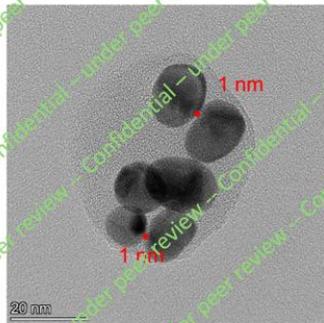
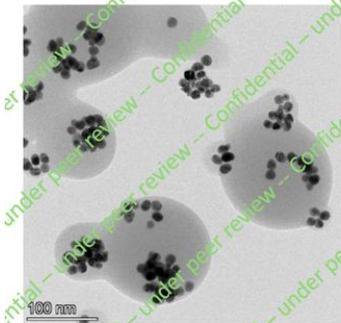
- **Breakthrough:** Our 2D CNN model can differentiate all stages of CCA (Normal, Inflammation, Pre-Cancer, Tumor), something classical ML cannot do.
- **Accuracy:** This SERS-based method shows high accuracy for *early* detection.
- **Future:** This technology is suitable for development into a point-of-care mobile application.

# Project activities: ENKKU: Biosensing platform based on SERS

## Surface Enhance Raman Spectroscopic (SERS) chip development

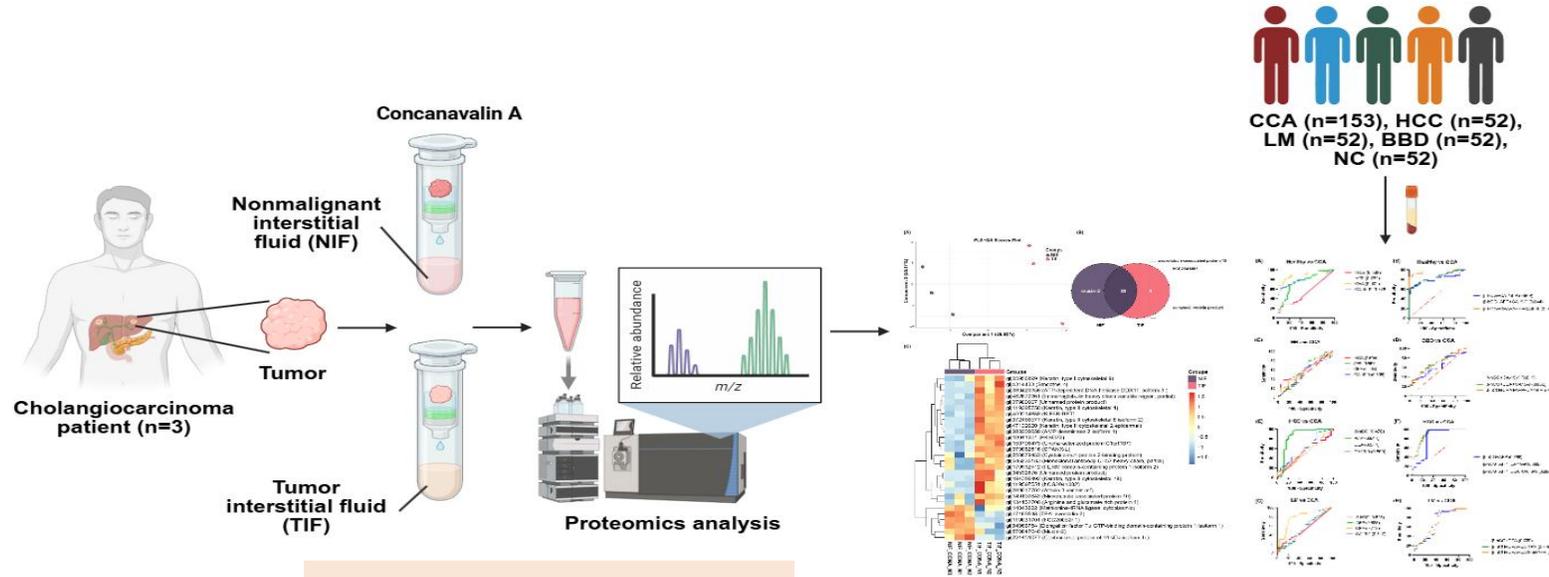
Part I: Synthesis of AuNPs and novel techniques to pair nanoparticles to yield greatest enhancement

1. Software license
2. (Q1) ACS OMEGA
3. (Scopus-index) Conference paper to appear in IEEEXplore

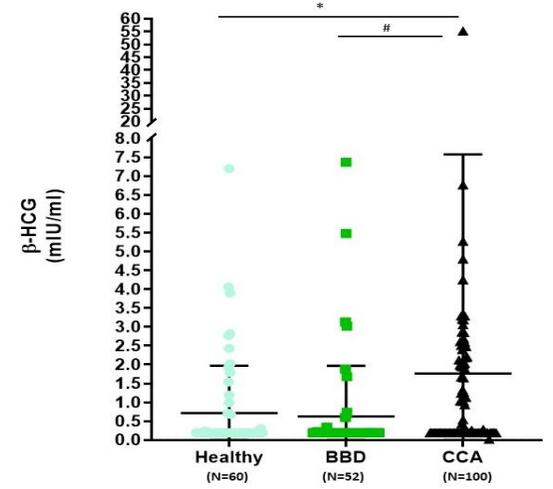


+ carried out characterization on TEMs, SEM, processing technique, etc. (Figures will be licensed under publisher)

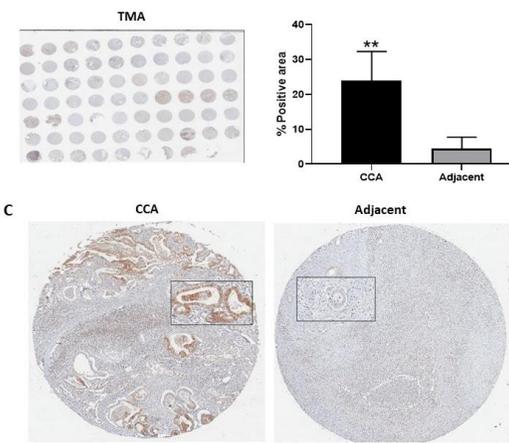
# Project activities: MDKKU-BIOTECH; Sample collection, identification and evaluation of biomarker in CCA patients



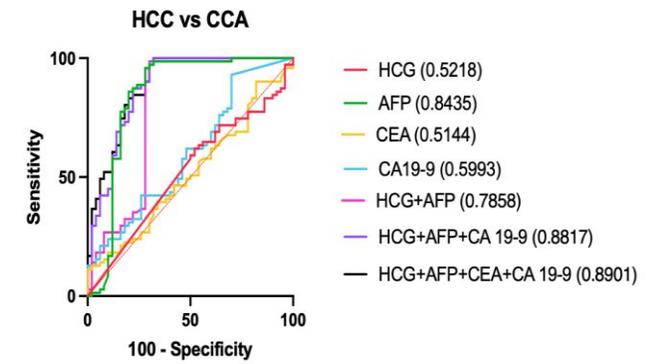
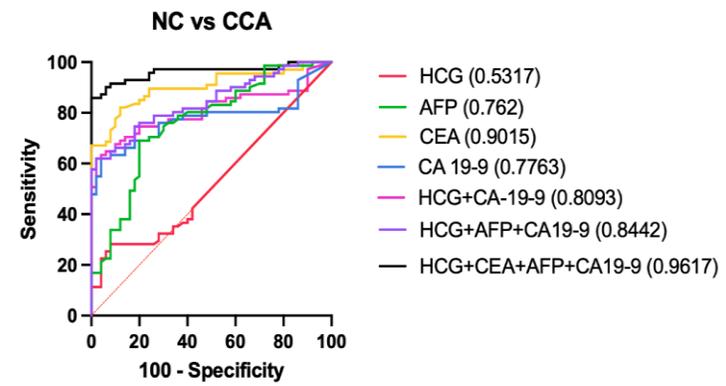
Flow chart of the study



Determine beta HCG level by automate



Verify beta-HCG expression in CCA array by IHC technique

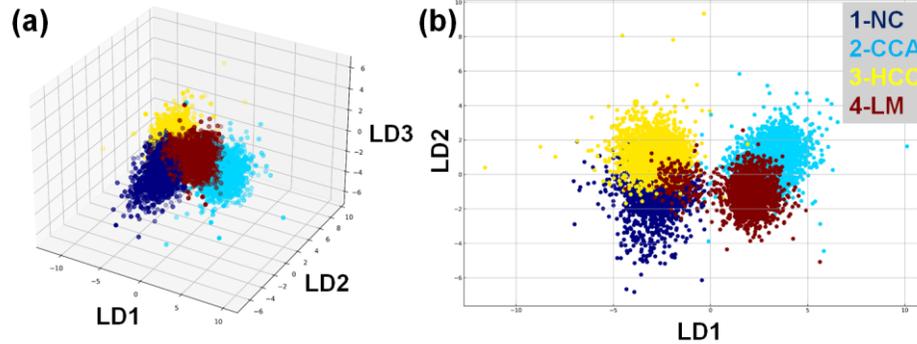
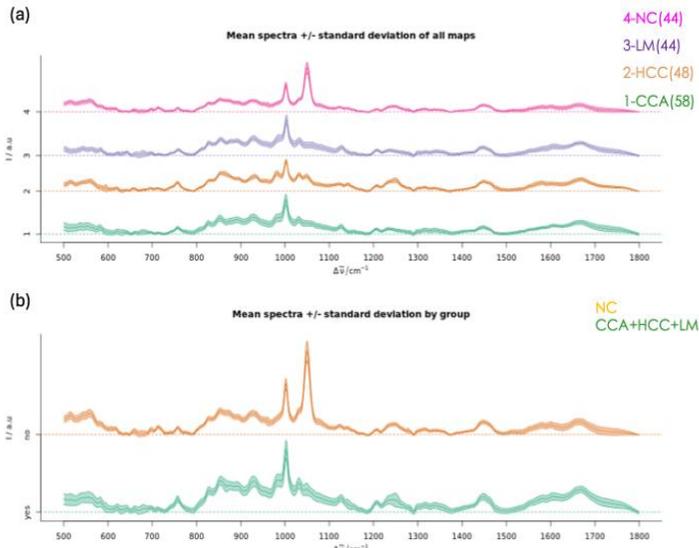


ROC analysis for the efficacy of its performance by compare/combine with routine biomarkers.

# Project activities: MDKKU/NECTEC; Raman spectrum detection and Machine learning training

Combination of Label-Free SERS-Based Nanosensors and Machine Learning for Diagnosis of Cholangiocarcinoma

Human samples analysis (n=221): CCA = 71, HCC = 50, LM = 50, HA = 50



LDA Achieves Superior Separation of Liver diseases

**(a) PCA (3D Plot):**

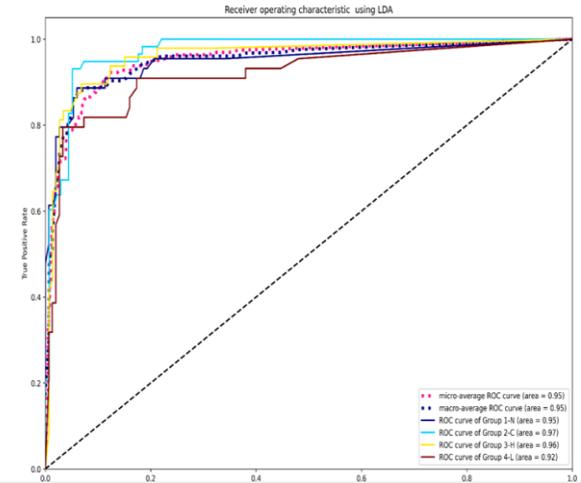
- Shows some natural clustering, but with significant overlap between groups.
- Visualizes spectral data for all four groups (NC, HCC, CCA, LM).

**(b) LDA (2D Plot):**

- Applied specifically to maximize class separability.
- Achieves **distinct and clear clustering**, effectively distinguishing all four groups.

LDA is a more powerful tool than PCA for classifying these spectral data.

SERS+LDA Model: High-Accuracy CCA Differentiation  
81% accuracy and 0.97 of AUC values.



LDA Model Achieves High Classification Accuracy

- **ROC Curves:** Evaluate the LDA model's ability to differentiate the four groups (NC, HCC, CCA, LM).
- **High AUC Values:** The Area Under the Curve (AUC) for each class is high, indicating excellent separation.
- **Strong Performance:** The model significantly outperforms a random classifier (diagonal line).

The SERS with LDA model is highly effective for accurate liver cancer detection.

Valid data (n=194) : CCA = 58, HCC = 48, LM = 44, HA = 44  
 SERS Distinguishes Healthy vs. Malignant Liver Tissue

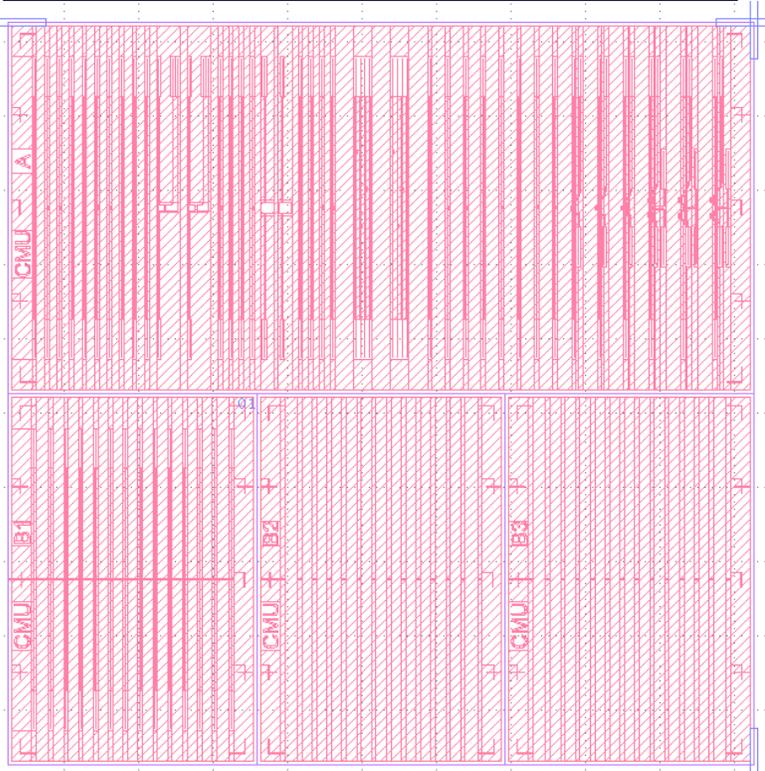
- (a) Group Comparison: Unique mean spectra for Normal, HCC, CCA, and LM.
- (b) Cancer vs. Normal: Significant spectral shifts identified between healthy (NC) and combined cancer (HCC+CCA+LM) samples.

Key Raman shifts can be used to distinguish healthy from malignant liver tissue.

# 2024 PROGRESS

## CMU: Biosensing platform based on silicon photonic development

### Fabrication of silicon photonic sensors



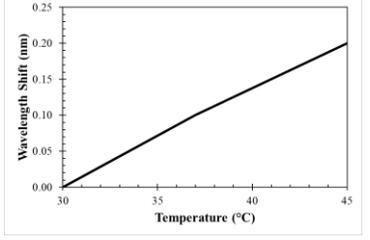
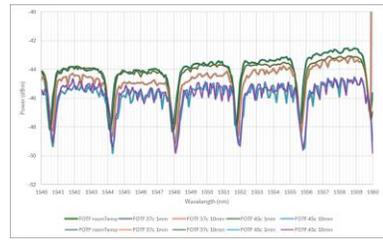
Photomask designs submitted to manufacturer (TMEC) **August 2024**

Fabricated sensors expected by **March 2025**

### Development of New sensor measurement system prototype

#### Proof of concept In Laboratory

broadband source



MEMS filter

Power Meter

**September 2024**

#### Measurement system prototype and sensors purchase order

**October 2024 – March 2025**

The project will order a developer to create a system based on the laboratory concept with software control

#### Tech transfer (workshop in CMU, demo of the prototype)

#### CCA detection test (Pending samples provided by KKU and Laos Team)

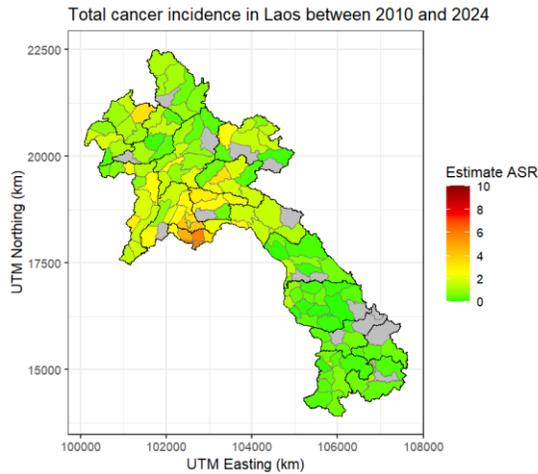
**February 2025**

COMPLETED

# Project activities: **LAOS** ; Biosensing platform for clinical application

## Biosensing potable platform for clinical sample of Laos CCA patients in various specimens

### Spatial Distribution of Cancer Cases in Hospital registries in Laos PRD

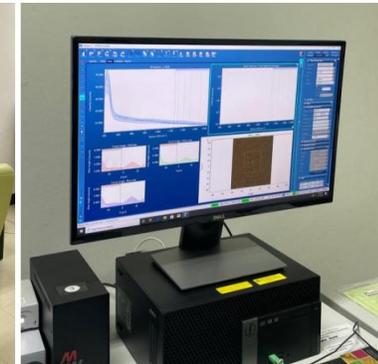
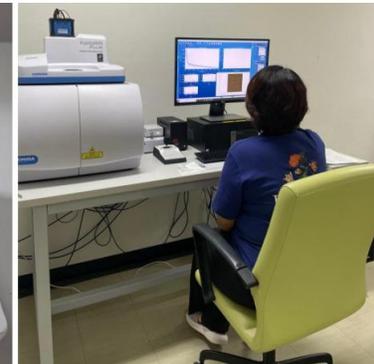


### 5. Transfer technology of SERS and AI for CCA diagnosis to Laos' team

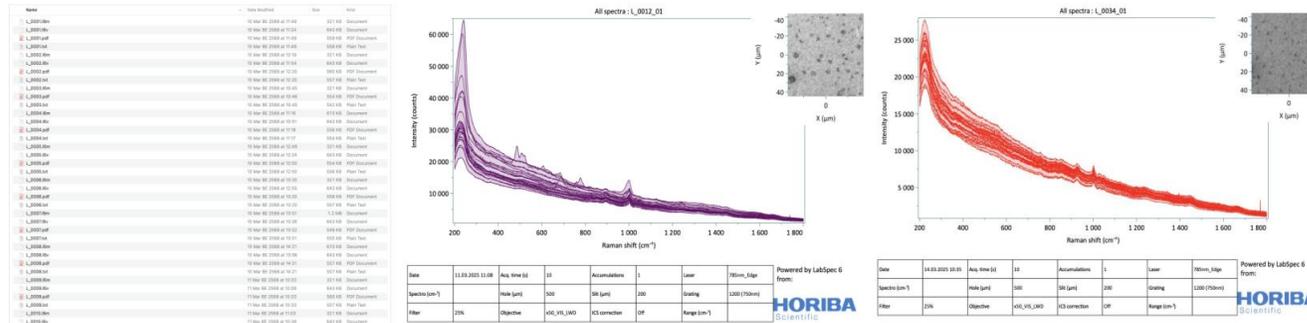
Transportation Laos' samples to KKU



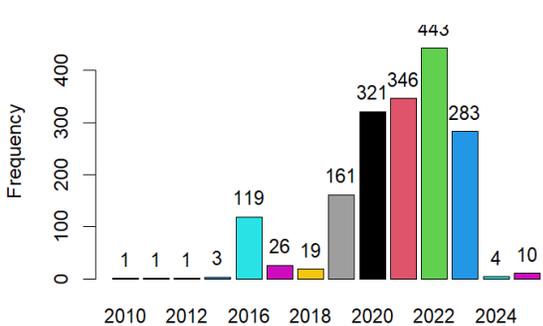
Detection of Serum Using Raman Spectroscopy



The raw Raman data and an example of the Raman peak results.



Distribution of dat.laos\$year



## Phase II



# Project activities: **Workshop on Nov 13-16, 2023 at Vientiane, LAOS**





# Project activities: **Workshop on Feb 18, 2025 at CMU, Thailand**

**18 FEB 2025**  
8:30 - 15:00

**WORKSHOP FOR INNOVATION OF PHOTONIC & ELECTROCHEMICAL BIOSENSORS FOR CHOLANGIOCARCINOMA DIAGNOSIS**

The workshop provides a comprehensive update on cholangiocarcinoma (CCA) research and the latest developments in electrochemical and photonic biosensors. It also serves as the conclusion of the ASEAN IVO project. The ICT Virtual Organization of ASEAN Institutes and NICT (ASEAN IVO) stand as a global alliance of ICT R&D institutes and the universities across the ASEAN region and Japan.

**SPEAKERS**  
Speaker Name and Titles

- PROF. NIPON THEERA-UMPON**  
CHANG MAI UNIVERSITY
- PROF. SOMCHAI PINLAOR**  
KHON KAEN UNIVERSITY
- DR. CHAMPADENG VONGDALA**  
CANCER CENTER, LAOS
- DR. PITAK EIAMCHAI**  
NATIONAL ELECTRONICS AND COMPUTER TECHNOLOGY CENTER
- DR. SITTIRUK ROYTRAKUL**  
NATIONAL CENTER FOR GENETIC ENGINEERING AND BIOTECHNOLOGY
- DR. CHAVIS SRICHAN**  
KHON KAEN UNIVERSITY
- DR. UKRIT MANKONG**  
CHANG MAI UNIVERSITY
- DR. NITHI ATTHI**  
THAN MICROELECTRONICS CENTER (INVITED SPEAKER)
- DR. YOSHINARI AWAJI**  
NATIONAL INSTITUTE OF INFORMATION AND COMMUNICATIONS TECHNOLOGY

Sponsored by **iRCT**



# Project activities: ASEAN IVO project review & report at LAOS and Cambodia

ASEAN IVO Forum 2023, 15-16 Nov 2023



6 months Review & Report, 15-16 Nov 2023, LAO



ASEAN IVO Forum 2024, 7-9 Nov 2024, Camdodia



1<sup>st</sup> Year Review & Report, 7-9 Nov 2024, at Phnom Penh



## Project activities: **Progress review at CMU, Thailand**



Dr.Emoto Hiroshi (NICT)  
Yoshihiro Sakuda (NICT Asia center, BBK, Thailand)  
Assoc.Prof.Sansanee Auephunviriyakul (CMU)  
Assoc.Prof.Ukrit Mankong (CMU)  
Dr.Suruk Udomsom (CMU)  
Prof.Somchai Pinlaor (KKU)

Group discussion at CMU, 27 Dec 2024



# Three directors of NICT have visited and discussed at MD-KKU for next project activity.



NICT

20 November 2024

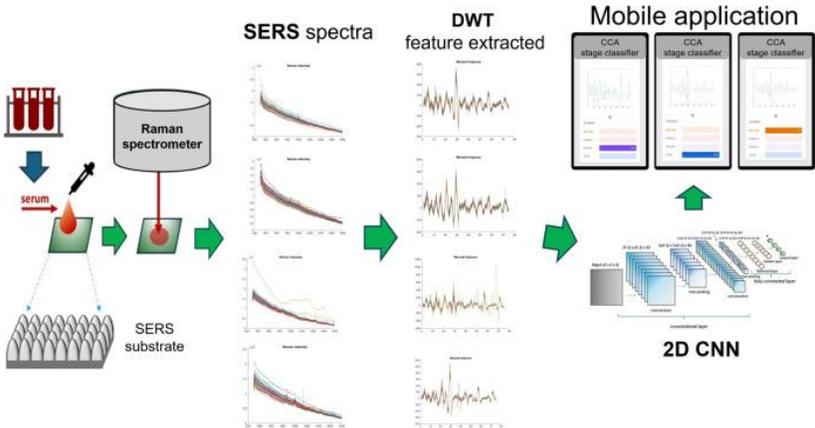
1. **Hiroaki Harai** (Director General of Network Research Institute)
2. **Tetsuya Kawanishi** (Research Executive Director, Prof. of Waseda University)
3. **Yoshinari Awaji** (Director General of Photonic ICT Research Center)
4. **Kouichi Akahane** (Director of Optical Access Technology Laboratory)
5. **Toshimasa Umezawa** (Senior Researcher of Optical Access Technology Laboratory)
6. **Atsushi Matsumoto** (Senior Researcher of Optical Access Technology Laboratory)





# Output/Outcome: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

## ENKKU: SERS chip development



The 2024 Biomedical Engineering International Conference (BMEICON-2024)  
**Early-Stage Cholangiocarcinoma Detection Using Surface-Enhanced Raman Spectroscopy and 1D CNN with Discrete Wavelet Transform**

**Pobpon Danviruta\***  
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 pobpa@kku.ac.th

**Sattra Wongthanasu**  
 College of Computing, Khon Kaen University, Khon Kaen, 40002, Thailand

**Somchai Pinaor**  
 Department of Parasitology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

**Chawalit Pairojok**  
 Department of Parasitology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

**Chavis Srirachan\*\***  
 Computer Engineering department and Biomedical Engineering department, Faculty of Engineering, Khon Kaen University, 40002, Thailand  
 chavis@kku.ac.th

**Abstract**—This Early detection of cholangiocarcinoma (CCA) is critical for improving patient prognosis and survival rates. Surface-Enhanced Raman Spectroscopy (SERS) offers a promising non-invasive diagnostic tool due to its high sensitivity and specificity. In this study, we propose a novel approach combining Discrete Wavelet Transform (DWT) and a one-dimensional Convolutional Neural Network (1D CNN) for the detection and differentiation of five stage CCA from precancerous, inflammation, and healthy states using SERS data. Our method is compared with a traditional Principal Component Analysis (PCA) followed by Support Vector Machine (SVM) classification. In contrast, the PCA+SVM method could only differentiate late-stage CCA and healthy states due to the nonlinearity of the SERS dataset. Receiver Operating Characteristic (ROC) curve analysis further validates the superior performance of our proposed method. We studied on hamster serum and the concept can be extended to human serum in the near future work.

**Index Terms**—Cholangiocarcinoma detection, Early stage CCA, SERS, Wavelet transform, 1D CNN

**1. INTRODUCTION (HEADING 1)**  
 Cholangiocarcinoma (CCA), a malignant tumor of the biliary tract, poses significant diagnostic challenges due to its asymptomatic nature in early stages and aggressive progression. Most detectable cases are in late-stage yielding low mortality rate. Early detection using effective treatment and improved patient outcomes [1]. Surface-Enhanced Raman Spectroscopy (SERS) has emerged as a powerful tool for biomedical diagnostics, offering molecular-level information with high sensitivity [2,7]. However,

differentiating early-stage CCA from precancerous, inflammatory, and healthy conditions remains challenging due to the subtle spectral differences and nonlinear characteristics of the SERS data.

Machine learning techniques have been applied to SERS data for cancer detection, with methods such as Principal Component Analysis (PCA) combined with Support Vector Machines (SVM) showing promising results [9]. Nevertheless, PCA+SVM approaches often struggle with nonlinear datasets, limiting their ability to distinguish between early-stage CCA and other conditions. Deep learning, particularly Convolutional Neural Networks (CNNs), has demonstrated superior performance in handling complex, nonlinear data in various pattern recognition tasks.

**II. RELATED WORK**  
 The application of Raman spectroscopy in cancer diagnostics has been extensively studied over the past decades. Raman spectroscopy provides a molecular fingerprint of biological samples, making it a valuable tool for disease detection. Surface-Enhanced Raman Spectroscopy (SERS) in particular, enhances the Raman signal by several orders of magnitude, allowing for the detection of low-concentration biomarkers [9,12]. Report on SERS in CCA detection could be rarely found in literature. Here are the list of work related to this study.

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 Authorized licensed use limited to: Khon Kaen University. Provided by Lintell. Downloaded on October 19, 2023 at 09:23:30 UTC from IEEE Xplore. Restrictions apply.



## Highly Accurate and Robust Early Stage Detection of Cholangiocarcinoma Using Near-Lossless SERS Signal Processing with Machine Learning and 2D CNN for Point-of-care Mobile Application

**Pobpon Danviruta<sup>1</sup>, Thatsanapong Pongking<sup>2</sup>, Suppakrit Kongsintaweek<sup>3</sup>, Somchai Pinaor<sup>4</sup>, Sattra Wongthanasu<sup>5</sup>, and Chavis Srirachan<sup>6</sup>**

**Cite This:** ACS Omega 2025, 10, 11296–11311

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**ABSTRACT:** Introduction: Cholangiocarcinoma (CCA), a malignancy of the bile ducts, presents a significant health burden with a notably high prevalence in Northeast Thailand, where its incidence rate is 85 per 100,000 population per year. The prognosis for CCA patients remains poor, particularly for proximal tumors, with a dismal 5-year survival rate of just 10%. The challenge in managing CCA is exacerbated by its typically late detection, contributing to a high mortality rate. Current screening methods, such as ultrasound, are insufficient, as many CCA patients do not exhibit prior symptoms or detectable liver fluke (*Ophiorhynchus viverrine*, OV) infections, underlining the urgent need for alternative early detection methods. Methods: In this study, we introduce a novel approach utilizing surface-enhanced Raman spectroscopy (SERS) combined with near-lossless signal compression via discrete wavelet transform (DWT) together with 2D CNN for the first time. Hamster serums of different stages were collected as the data set. DWT was employed for feature extraction, enabling the capture of the entire SERS spectrum, unlike traditional methods like PCA and LDA, which focus only on specific peaks. These features were used to train a 2D convolutional neural network (2D CNN), which is particularly robust against translation, rotation, and scaling, thus effectively addressing the SERS peak shifting issues. We validated our approach using gold-standard histology, and notably, our method could detect CCA at an early stage. The ability to identify CCA at the early stage significantly improves the chances of successful intervention and patient outcomes. Results and conclusions: Our results demonstrate that our method, combining SERS with extremely compact wavelet feature extraction and 2D CNN, outperformed other approaches (PCA+SVM, PCA+1D CNN, PCA+2D CNN, LDA+SVM, and DWT+1D CNN), achieving performance of 95.1% accuracy, 95.08% sensitivity, 98.4% specificity, and an area under the curve (AUC) of 95%. The trained model was further deployed on a server and mobile application interface, paving the way for future field experiments in rural areas and home-use potential point-of-care services.



## Minimally invasive detection of early-stage opisthorchiasis-associated cholangiocarcinoma using label-free surface-enhanced Raman spectroscopy (SERS) of hamster serum

**Apilich Chaidee<sup>1,2</sup>, Suppakrit Kongsintaweek<sup>3,4</sup>, Thatsanapong Pongking<sup>5</sup>, Keerapach Tanbungrasri<sup>6</sup>, Aye Myat Mori<sup>7</sup>, Chawalit Pairojok<sup>8</sup>, Pakornrat Tanasaka<sup>9,10</sup>, Tatyakorn Piangpakart<sup>11</sup>, Kessana Na-Bangchang<sup>12</sup>, Naruechar Charoensam<sup>13</sup>, David Blair<sup>14</sup>, Somchai Pinaor<sup>15,16</sup>**

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**OPEN ACCESS**  
 Citation: Chaidee A, Kongsintaweek S, Pongking T, Tanbungrasri K, Mori AM, Pairojok C, et al. (2025) Minimally invasive detection of early-stage opisthorchiasis-associated cholangiocarcinoma using label-free surface-enhanced Raman spectroscopy (SERS) of hamster serum. PLoS One 20(25): e0334918. <https://doi.org/10.1371/journal.pone.0334918>

**Abstract**  
**Background**  
 Cholangiocarcinoma (CCA) is a deadly cancer often detected late. Current diagnostic methods, such as ultrasound and invasive biopsies, have limitations; there is a critical need for a rapid, minimally invasive and effective strategy for the early diagnosis and staging of CCA.

**Methods**  
 We aimed to address this need using serum samples and label-free surface-enhanced Raman spectroscopy (SERS) combined with machine learning. CCA development was induced in hamsters using a combination of *Opisthorchis viverrini* infection and administration of *N-nitrosodimethylamine*, with induction time courses spanning 1–6 months. Normal and pathological stages (inflammation, precancerous lesion, and CCA) were assigned based on histopathological features, as well as the expression of cytokeratin 19 and alpha-fetoprotein. Raman spectra were subjected to dimensional reduction using principal component analysis, and diagnostic clusters were acquired using partial least-squares discriminant analysis.

**RESEARCH ARTICLE**  
**OPEN ACCESS**  
 Citation: Chaidee A, Kongsintaweek S, Pongking T, Tanbungrasri K, Mori AM, Pairojok C, et al. (2025) Minimally invasive detection of early-stage opisthorchiasis-associated cholangiocarcinoma using label-free surface-enhanced Raman spectroscopy (SERS) of hamster serum. PLoS One 20(25): e0334918. <https://doi.org/10.1371/journal.pone.0334918>

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PLOS ONE | <https://doi.org/10.1371/journal.pone.0334918> October 27, 2025

1. One license for SERS signal processing using multiresolution compression and convolutional neural networks
2. Sharing proteomics data: The accession numbers are PXD057256 for ProteomeXchange and JPST003438 for jPOST.
3. Sharing Raman data : Mendeley: DOI: 10.17632/8gs6tc6vgr.1 (Animal); Mendeley: DOI:10.17632/hzg43f63k9.1. (Human)

หนังสือแนบเอกสารแจ้งข้อมูลลิขสิทธิ์  
 ออกให้เพื่อแสดงว่า  
 มหาวิทยาลัยขอนแก่น  
 ได้แจ้งข้อมูลลิขสิทธิ์ไว้ก่อนการนำข้อมูลไปประยุกต์ใช้

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 (bioRxiv) และ Desktop Application for Raman Signal Classification  
 for Cholangiocarcinoma Stage Identification using Multiresolution  
 Feature Extraction and Deep Neural Networks)

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ลงชื่อ.....  
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### Surface-enhanced Raman spectroscopy and machine learning differentiate specific liver cancers

Journal:	ACS Applied Nano Materials
Manuscript ID:	Draft
Manuscript Type:	Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Intuyod, Kitt; Khon Kaen University Faculty of Medicine Kongsintaweek, Suppakrit; Khon Kaen University, Biomedical sciences program, Graduate school Eiamchai, Pitak; National Electronics and Computer Technology Center, Luvira, Vor; Khon Kaen University, Department of Surgery, Faculty of Medicine Chaidee, Apisit; Khon Kaen University, Department of Parasitology, Faculty of Medicine Techaeman, Anchalee; ; Khon Kaen University, Centre for Research and Development of Medical Diagnostic Laboratories, Faculty of Associated Medical Sciences, Pinaor, Porrtip; Khon Kaen University Pairojok, Chawalit; Khon Kaen University, Department of Pathology, Faculty of Medicine Blair, David; James Cook University Umezawa, Toshimasa; National Institute of Information and Communications Technology (NICT) Matsumoto, Atsushi; Kyushu University Akahane, Kouichi; National Institute of Information and Communications Technology horahatsum, mab; National Electronics and Computer Technology Center, Opto-Electrochemical Sensing Research Team Limwichian, Sakson; National Electronics and Computer Technology Center Nuntawang, Noppadon; National Electronics and Computer Technology Center, Pinaor, Somchai; Khon Kaen University, Department of Parasitology

### Advances in Medical Sciences Development and clinical validation of a $\beta$ -HCG-based panel for cholangiocarcinoma screening: from proteomics to clinical validation

Manuscript Number:	Original Article / Research	
Article Type:	Original Article / Research	
Keywords:	Bile-duct cancer, Biomarker, Liver cancer, Tumor interstitial fluid	
Corresponding Author:	Porrtip Pongking, PhD Khon Kaen University THAILAND	
First Author:	Suppakrit Kongsintaweek	
Order of Authors:	Thatsanapong Pongking Sudarat Omsawatthum Chawalit Pairojok Kiti Intuyod Vor Luvira David Blair Somchai Pinaor Porrtip Pongking, PhD	
Abstract:	Purpose: Opisthorchis viverrini-associated cholangiocarcinoma (CCA) in Northeast Thailand is marked by late diagnosis and poor prognosis, creating a critical need for effective early-detection biomarkers. This study aimed to identify a novel glycoprotein biomarker panel from tumor interstitial fluid (TIF) to improve CCA screening. Materials/Methods: Glycoprotein-enriched TIF and paired normal interstitial fluid samples from three CCA patients were analyzed using immunoprecipitation-liquid mass spectrometry (IP-LC-MS/MS). Given its increase in various cancers, the protein abundance of beta-human chorionic gonadotropin (beta-hCG) was assessed using immunohistochemistry (IHC) in a tissue array of 100 CCA samples. Serum levels of beta-hCG, carbohydrate antigen 19.9 (CA 19.9), alpha-fetoprotein (AFP), and carcinoembryonic antigen (CEA) were quantified in 405 individuals, including patients with CCA (n=173), other hepatobiliary diseases, and healthy controls. Performance of beta-hCG in screening for CCA was evaluated. Results: Proteomic analysis identified elevated beta-hCG specificity in TIF from CCA patients. IHC confirmed significantly higher beta-hCG expression in tumor tissues compared to adjacent non-tumor areas (p<0.001). Serum beta-hCG levels were significantly increased in CCA patients and correlated with tumor volume and reduced (p<0.001). While beta-hCG alone had limited diagnostic performance, a combined panel adding CA 19.9, CEA, and AFP yielded excellent diagnostic accuracy (AUC: 0.92; sensitivity: 88%; specificity: 100%). Conclusions: beta-hCG is a valuable prognostic marker for CCA and is a multi-marker (CA 19.9, CEA, AFP) panel with excellent diagnostic performance. This panel shows strong potential for application in early-stage diagnosis and prognosis evaluation of CCA, warranting large-scale validation for clinical application.	
Opposed Reviewers:		



# Future works:



Thailand



สถาบันวิจัยระบบสาธารณสุข

Lao PDR

Phase II



## Lancang - Mekong Cooperation

澜沧江 - 湄公河合作

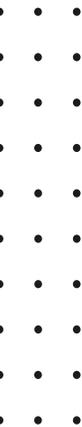
Thailand---Lao PDR---China

## Greater Mekong subregion



## Conclusion: Innovation of photonic and electrochemical biosensors for cholangiocarcinoma diagnosis

1. **Target:** This study aims to develop and validate innovative optical and electrochemical biosensing platforms for the early diagnosis of cholangiocarcinoma.
2. **Methods:** We used SERS and AI, proteomic, silicon photonics platform.
3. **Scientific papers:** 3 international published, 2 international under revised/review
4. **Societal impact:** Our data Raw data are available to publish access. This technology is ongoing to implement in Lao PDR in Phase II project.
5. **New partners:** We have new collaborative partner including NECTECT, BIOTECH from Thailand, Philippines, and China.
6. **Collaborative:** We have expanded of the larger cohort to study in Thailand, Lao, and China.



# Thank you



*Cancer Center Lao PDR*

*Est. 2017*



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