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Investigator-Initiated Research Proposals for Small Extramural Grants - 2025

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Proposal Id: IIRPSG-2025-01-05081, **Version Id:** F1,
Proposal Title: Developing a Surface Enhanced Raman Spectroscopy based multiplex detection platform to predict DCIS invasiveness using selected biomarkers derived from comparative analysis of DCIS and IDC

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Nature of Employment	Permanent
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Proposal Details PART-A

Nature of employment in Medical Institutes, Research Institutes, Universities, Colleges, recognized Research & Development laboratories, Government and semi-government organizations, and NGOs.	Permanent
Advertisement	Call for Investigator-Initiated Research Proposals for small extramural grants - 2025

Summary (up to 250 words): A structured summary should contain the following subheadings: Rationale/ gaps in existing knowledge, Novelty, Objectives, Methods, and Expected outcome. Ductal carcinoma in situ (DCIS) is a non-invasive precursor to breast cancer, characterized by abnormal epithelial cell growth within mammary ducts, accounting for 20-25% of new breast cancer cases. Identifying biomarkers to predict its invasive potential is crucial for precision treatment, but no established predictive panel exists to date. The present study is focused on the development of a multiplex detection platform for the biomarkers in DCIS using Surface Enhanced Raman Spectroscopy (SERS) after initial screening with Immuno-histochemistry (IHC). For this, DCIS and Invasive ductal carcinoma (IDC) samples will be screened first by IHC followed by SERS for the prevalence of ER, PR and HER-2 receptors to get a statistical output. Further, by comparing the samples across receptor subtypes for key biomarkers viz., p53, p16, p21, FGF-2, FAP- α , COX-2, NF- κ B, TGF- β , and epithelial-mesenchymal markers like N-cadherin and vimentin, this study aims to identify biomarkers linked to invasiveness and correlate them with hormonal receptor status and to select a predictive panel. Multiplex SERS analysis will be performed with these selected biomarkers as a cost effective, time and sample conserving detection modality. Gold nanoparticles conjugated with a Raman reporter and specific monoclonal antibodies will bind to biomarkers in tissue samples, producing signature peaks in Raman analysis. This enables semiquantitative receptor status assessment, prevailing over the subjective nature of IHC. The expected outcome of this work is the development of a biomarker set and a SERS based multiplex detection platform to predict the invasive nature of DCIS.

Priority Area/Priority Area diseases	Non-Communicable Diseases / Cancer
Keywords Six keywords separated by comma which best describe your project may be provided.	DCIS, IDC, biomarker, Invasiveness, SERS, Multiplex-detection
Abbreviations Only standard abbreviations should be used in the text. List of abbreviations maximum of ten may be given as a list.	DSIC - Ductal Carcinoma in situ IDC - Invasive ductal carcinoma SERS - Surface enhanced Ramna spectroscopy FFPE – Formalin fixed paraffin embedded BM – Biomarker RR – Raman reporter ER – Oestrogen receptor PR – Progesterone receptor HER-2 – Human Epidermal growth factor recetor 2 AuNP – Gold nanoparticles PEG – Polyethylene glycol

Problem Statement (up to 500 words): State the currently available information to present the problem adequately.

DCIS is a pre-invasive form of Breast cancer having probability to develop into invasive ductal carcinoma (IDC)(Visser et al. (2019). Highly heterogenous nature of DCIS varies from slow-growing, dormant types to more aggressive forms that can quickly progress to invasive IDC. DCIS accounts for 20–25% of newly diagnosed breast cancer, where approximately 40 % of woman treated with excision and radiotherapy can develop recurrence and half of it may progress to ICD (Shee et al., 2019,.Provenzano et al., 2003) The unpredictable nature of DCIS may also lead to receive aggressive treatments by DCIS patients even if they don't have the chances to develop IDC. Without screening programs that can accurately identify high-risk cases, over-treatment will persist (Visser et al., 2019). At the same time, observations suggest a significant recurrence rate following breast-conserving surgery for DCIS, with a 40-50 % of these cases progressing to life-threatening IDC (Pawloski et al., 2021). As if now, there are no established biomarkers or techniques to predict the progressive nature of DCIS, which can benefit the patient to receive the precise treatment. Reports suggests that, low ER and PR status can be correlated with the invasive nature of DCIS (Sänger et al., 2014), whereas HER-2/neu over expression is reported to be a predictor for invasive transition of DCIS (Miligy et al., 2019). Finding a correlation between these receptor status and markers involved in the cell proliferation, invasion, and inflammatory mediators may lead to evolve a panel of biomarkers which can be relied to predict the progressive nature of DCIS and it is reported that, epithelial mesenchymal transition may be involved in the DCIS progression to invasive basal-like breast cancers (Wang et al., 2019). Regarding the technique employed to track the expression profiles of these proteins in the DCIS tissue specimens, IHC serves as the gold standard. The inherent subjective nature and difficulty in quantifying and multiplexing remains as the major drawbacks of IHC (Verma, 2022). Utilising Surface enhanced Raman spectroscopy mediated detection modality for biomarkers can offer a semiquantitative detection platform based on the intensity profile and the narrow band width of SERS signals can offer the multiplexing. Here in this proposal, we are aimed to screen the FFPE samples of pure DCIS or DCIS components in IDC comparing with IDC to verify the correlation between the basic receptor protein expression and selected biomarkers reported to be involved in the DCIS progression to evolve a panel of predictor biomarkers. This stratification will aid in the development of personalized treatment strategies. Introduction of SERS multiplex platform for the screening of this biomarker panel can serve as a rapid, cost effective and sample saving detection modality.

Rationale of the study (up to 500 words) Mention how the research question addresses the critical barrier(s) in scientific knowledge, technical capability, and/or programmatic/ clinical/lab practice and its relevance to local, national and international context with relevant bibliography.

Being the most common female cancer type in India, early detection of breast cancer is of prime importance as it can effectively manage disease progression, significantly improves survival rates and treatment outcomes. DCIS is a non-invasive breast lesion with abnormal cells remain confined within the duct which can be considered as a precursor to invasive breast cancer. There are 20-30 % chances of developing DCIS in to ICD. Despite this, clinical management typically involves treating all patients for the risk of progression, leading to the potential overtreatment of many individuals. Histological classification systems categorize DCIS based on factors such as nuclear atypia and necrosis to assess the likelihood of progression or recurrence as invasive cancer. However, even low-risk DCIS has the potential to progress, though it may take longer to do so (Hayward Weaver, 2021). Along with histological grading, ER, PR and HER-2 receptor immunohistochemistry has been followed for deciding the treatment regimens (Meijnen et al., 2008). There is an urge to facilitate the accurate identification of the progressive nature of DCIS to establish the prognostic outcome and effective management. Biomarkers play a crucial role in detecting the aggressive nature of DCIS, but there is no such decisive biomarker or panel of biomarkers has been reported till date to be implemented in clinics. SERS being a highly sensitive technique, with narrow bandwidth has the potential to screen the biomarkers more rapidly and efficiently. Our hospital component is having the facility for the automated IHC analysis to identify the prevalence of biomarkers in DCIS subtypes. Similarly, the team has already proven the SERS based multiplex detection of biomarkers in FFPE breast cancer tissue samples and the technique has been patented also. Our objective is to develop a panel of predictive biomarkers for DCIS progression based on the IHC analysis of the expression profiles of ER, PR and HER-2 receptor and the selected biomarkers involved in cell proliferation, inflammation and invasion in comparison with IDC samples. The biomarker selection was carried out on the basis of literature survey, where its relevance in DCIS progression is specified (Davis et al., 2015 Dettogni et al., 2020 Lari Kuerer, 2011 Provenzano et al., 2003b). The co-validation of these biomarker panel can be semi-quantitatively performed using specific SERS nanotags. The intra-observer error and non-multiplexing nature of IHC can be resolved by introducing the SERS based multiplex detection platform. As our team has already demonstrated the multiplex detection of ER, PR and HER-2 using SERS analysis in invasive breast cancer FFPE specimens, this can be translated into the new set of biomarkers which can complement the IHC analysis. By combining the multiplexing SERS platform and a decisive biomarker panel, DCIS patients can be benefited from under or over treatment regimens.

Hypothesis/ Research question (up to 100 words) : • What is the expression status of ER, PR and HER-2 in DCIS in Indian scenario. • Do the hormonal receptor status correlates with DCIS progression • Which key biomarkers are getting under or over expressed during DCIS progression • Is it possible to develop a predictive biomarker panel for DCIS invasiveness • Correlation between hormonal receptors with biomarkers involved in proliferation and invasion • Do the SERS nanotags can be efficiently employed for the multiplex detection these biomarkers in DCIS specimens.

Methodology

Include objective-wise work plan under the following sub-headings:

Study Objective No. 1

Study Objective : Immunohistochemical analysis of DCIS and IDC tissues to evaluate the expression profiles of ER/PR/HER-2 and selected biomarkers involved in cell proliferation, inflammation and epithelial-mesenchymal transition.

Study Design : Study pattern -Cross sectional studies, sample - DCIS and IDC tissue samples, FFPE sections. During the first and second year, Institute will screen a total 62 numbers of patients with DCIS and IDC using trucut biopsy specimens. Initially, ER/PR and HER-2 expression status will be analysed using immunohistochemistry. Further, the expression pattern of the biomarkers involved in cell proliferation/cell cycle regulation (p53, p16, p21, FGF-2, Fibroblast associated protein- α), inflammatory pathways (COX- 2, NF- κ B, TGF - β) and N cadherin and vimentin as EMT markers will be studied by IHC. The selection of biomarkers is based on the available literatures on DCIS. DCIS component in IDC will also be analysed to examine the difference in biomarker profiles as compared to pure DCIS and IDC part.

Study Area : Hospital and Laboratory Hospital: Department of Oncology, Amala Institute of Medical Sciences, Thrissur, Kerala. Department of Pathology, Amala Institute of Medical Sciences, Thrissur

Sample Size : Sample size was estimated to be 31 samples per DCIS and IDC. Sampling technique – purposive sampling Two proportion sample size calculation method was followed based on the available literature So, Total samples - 62 No.s

Primary and secondary outcome measure : This will generate a statistical data regarding the prevalence of each biomarker in DCIS and IDC population. Correlation between these biomarker expressions under different pathological conditions can also be evaluated from the results of this study.

Design of Statistical analysis : Data were entered using Microsoft Excel and analyzed with SPSS version 23. The qualitative Variables are presented as percentages, while the quantitative variables are expressed as mean and Standard deviation. Student's t-test and ANOVA will be used to calculate statistically significant differences between the subtypes in IHC analysis and scoring.

Study Objective No. 2

Study Objective : To evolve a panel of biomarkers to predict the invasive nature of DCIS by comparative assessment with IDC to facilitate SERS based multiplex detection.

Study Design : Based on the screening of the 31 samples each from DCIS and IDC to evaluate the expression pattern of hormonal receptors and biomarkers like COX-2, p53, p16, p21, FGF-2, Fibroblast associated protein- α , TGF - β and epithelial-mesenchymal markers, a comparative evaluation will be performed. Staining pattern, percentage of positive cells and IHC scoring will be evaluated separately for each biomarker per sample. Based on this comparison, a panel of biomarkers having predictive role of invasiveness will be selected.

Study Area : Hospital/Laboratory Hospital: Department of Medical Oncology, Amala Institute of Medical Sciences, Thrissur, Kerala. Department of Pathology, Amala Institute of Medical Sciences, Thrissur

Sample Size : in objective 2 , there is no separate samples, the staining results obtained for samples mentioned in objective 1 will be evaluated in objective 2, that is 62 samples

Primary and secondary outcome measure : This will lead to the development of a predictive biomarker panel for DCIS progression. As secondary output, correlation between hormonal receptors and the selected biomarkers involved in cell proliferation, inflammation and invasion can also be established.

Design of Statistical analysis : Student's t-test and ANOVA will be used to calculate statistically significant differences between the subtypes in IHC analysis and scoring. Statistical analysis will be done using SPSS version 23.

Study Objective No. 3

Study Objective : Synthesis and characterization of SERS nanotags specifically targeting the selected panel of biomarkers to accomplish the SERS analysis and multiplex detection

Study Design : The objective will be initiated during the first year and will be continued to 2nd and third years. This will include the synthesis and characterisation of SERS substrate, Raman reporter selection to get non-overlapping, multiplex enabling SERS spectrum. Gold nanoparticle synthesised by citrate reduction method will be used as SERS substrate to which chemical entities with specific Raman signature peaks (Raman reporter) will be conjugated and covered with Polyethylene glycol. These substrates will be surface functionalised with specific monoclonal antibodies targeting the respective biomarker to get the SERS-nanotag. Each type of SERS nanotag will be having its own specific Raman peak and targeting monoclonal antibody. At first, the detection efficacy of the platform will be confirmed by screening ER/PR/HER-2 in IHC confirmed DCIS and IDC tissue subtypes. Further, with the selected biomarkers, SERS analysis will be conducted by singleplex, duplex and multiplex analysis to find out the sensitivity and specificity. Co-investigators from Chemical Sciences and Technology Division. CSIR-NIIST will be mentoring the SERS nanotag preparation, characterisation and analysis of DCIS tissue samples by Raman spectroscopy. IHC screened samples will be provided by the department of Pathology, Amala Institute of Medical Sciences.

Study Area : Laboratory Chemical Sciences Technology Division (CSTD), Organic Chemistry Section, CSIR-National Institute for Interdisciplinary Science Technology (CSIR-NIIST), Thiruvananthapuram.

Methodology

Include objective-wise work plan under the following sub-headings:

Sample Size : Same samples of objective 1 will be evaluated in objective 3 by SERS modality. Total 62 samples.

Primary and secondary outcome measure : Primary outcome will be the SERS nanotags specifically targeting the biomarkers and the optimized tissue analysis protocol including the equipment parameters like laser power, integration time, Raman mapping parameters etc. From this a diagnostic kit containing the cocktail of SERS nanotags can be prepared for the multiplex analysis of biomarkers. Thus, it can derive a SERS based diagnostic kit to monitor DCIS progression.

Design of Statistical analysis : Data analysis and processing were performed with WITec Project 5.2 Plus (v2.1) software package. The background noises were evaded and the spectral smoothing was done by a 4th polynomial function and Savitzky-Golay respectively. Student's t-test and ANOVA will be used to calculate statistically significant differences between the SERS spectral intensity in different samples. Data were entered using Microsoft Excel and analyzed with SPSS version 23. The qualitative Variables are presented as percentages, while the quantitative variables are expressed as mean and Standard deviation.

Expected outcome/ Deliverables aligned with research question (up to 100 words): With this project, we are expecting to develop a biomarker panel and a multiplex detection platform for predicting the invasive nature of DCIS specimens. This can benefit the patient to obtain precise treatment. The comparative analysis can lead to the identification of the potential candidate biomarkers whose expression profiles varies with invasives. SERS nanotag based Raman spectral scanning can cover the whole tissue specimen within 45 minutes to generate a mapped image showing the biomarker prevalence in the sample along with the spectral peaks.

Immediate next steps following the end of the project (up to 100 words): The feasibility and accuracy of the proposed method and biomarker panel will be evaluated pan India. Multicentric clinical trials will be conducted at different regions with special focus on regions where breast cancer burden is reported to be high like Tamil Nadu, Telangana, Karnataka, and Delhi.

Whether the study is going to generate new intellectual property: After performing sufficient number of clinical trials, the proposed platform can be developed as a diagnostic kit which can be presented for patent filing.

Reference in (AMA style): Davis, J. E., Nemesure, B., Mehmood, S., Nayi, V., Burke, S., Brzostek, S. R., & Singh, M. (2015). Her2 and Ki67 Biomarkers Predict Recurrence of Ductal Carcinoma in Situ. *www.appliedimmunohist.com* Dettogni, R. S., Stur, E., Laus, A. C., Da Costa Vieira, R. A., Marques, M. M. C., Santana, I. V. V., Pulido, J. Z., Ribeiro, L. F., De Jesus Parmanhani, N., Agostini, L. P., Dos Reis, R. S., De Vargas Wolfgramm Dos Santos, E., Alves, L. N. R., Garcia, F. M., Santos, J. A., Do Prado Ventorim, D., Reis, R. M., & Louro, I. D. (2020). Potential biomarkers of ductal carcinoma in situ progression. *BMC Cancer*, 20(1). <https://doi.org/10.1186/s12885-020-6608-y> Hayward, M. K., & Weaver, V. M. (2021). Improving DCIS diagnosis and predictive outcome by applying artificial intelligence. In *Biochimica et Biophysica Acta - Reviews on Cancer* (Vol. 1876, Issue 1). Elsevier B.V. <https://doi.org/10.1016/j.bbcan.2021.188555> Lari, S. A., & Kuerer, H. M. (2011). 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Predictors of an invasive breast cancer recurrence after DCIS: A Systematic Review and Meta-analyses. In *Cancer Epidemiology Biomarkers and Prevention* (Vol. 28, Issue 5, pp. 835–845). American Association for Cancer Research Inc. <https://doi.org/10.1158/1055-9965.EPI-18-0976> Davis, J. E., Nemesure, B., Mehmood, S., Nayi, V., Burke, S., Brzostek, S. R., & Singh, M. (2015). Her2 and Ki67 Biomarkers Predict Recurrence of Ductal Carcinoma in Situ. *www.appliedimmunohist.com* Dettogni, R. S., Stur, E., Laus, A. C., Da Costa Vieira, R. A., Marques, M. M. C., Santana, I. V. V., Pulido, J. Z., Ribeiro, L. F., De Jesus Parmanhani, N., Agostini, L. P., Dos Reis, R. S., De Vargas Wolfgramm Dos Santos, E., Alves, L. N. R., Garcia, F. M., Santos, J. A., Do Prado Ventorim, D., Reis, R. M., & Louro, I. D. (2020). Potential biomarkers of ductal carcinoma in situ progression. *BMC Cancer*, 20(1). <https://doi.org/10.1186/s12885-020-6608-y> Hayward, M. K., & Weaver, V. M. (2021). 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Proposal Details (PART-B)

Preliminary work done by the PI including the source of funding (up to 250 words): Study : Multiplex detection of hormonal receptors in breast cancer tissues Funded by : CSIR – Healthcare project Our previous studies demonstrated the SERS based multiplex detection of ER, PR and HER-2 in a ratiometric way using breast cancer FFPE samples. The study has been applied for Indian (PCT/IN2021/050577) and US patent (18041283, published on 2023/9/28) and is under published status. We analysed the retrospective breast cancer tissue samples using Gold nanoparticles (AuNP) as SERS substrate for the signal amplification. Raman reporters (RR), Crystal violet (CV), Squaraine Di Lipoic acid(SDL), Mercaptobenzoic acid(MBA) and Di-thionitro benzoic acid (DTNB) with signature peaks at 440, 580, 1080 and 1320 cm⁻¹, respectively were used to get the multiplex Raman peaks. PEG coating after RR addition enhanced the stability of the SERS nanotags to which BM specific monoclonal antibodies were attached for the specific binding to the hormone receptors in the tissue samples. To trace each BM, specific SERS nanotags with particular RR and respective monoclonal antibodies were employed viz., AuNPSDLER (to map ER), AuNPMBAPR (to map PR), AuNPCVHER-2 (to map HER-2) and AuNPDTNBisotype control (For ratiometric screening). Ratiometric analysis of singleplex, duplex, and triplex BM helped to mitigate the false positive results. Notably, sensitivity and specificity rates of 95% and 92% for singleplex, 88% and 85% for duplex, and 75% and 67% for triplex BM were achieved by analyzing the distinct Raman fingerprints of the respective SERS-tags. Furthermore, a semi-quantitative assessment of HER2 grading (4/2/1) in tissue samples was accomplished by Raman intensity profiling.

Skill and experience of the research team (Highlight only salient points (along with 5 relevant publications) that provides confidence to reviewers that team can implement the project with quality.) : Dr. Vishnu Priya Murali, recently joined as Scientist C at Amala Institute of Medical Sciences was the previous project scientist at CSIR-NIIST. She is a well experienced researcher and biologist with proven track to manage the biomarker analysis using both IHC and SERS platform. She has expertise in SERS nanotag synthesis and characterisation, SERS analysis using solid and liquid samples for biomarker detection and data interpretation. Similarly, she is experienced with the histological and molecular diagnostic technique with focus to develop cost effective diagnostic strategies suitable for our nation. She will be correlating the research activities at Amala and NIIST for the successful management of the project. Relevant publications 1. Murali VP, Karunakaran V, Murali M, et al. A clinically feasible diagnostic spectro-histology built on SERS-nanotags for multiplex detection and grading of breast cancer biomarkers. *Biosens Bioelectron.* 2023;227:115177. doi:10.1016/j.bios.2023.115177. 2. Karunakaran V, Saritha VN, Ramya AN, Murali VP, Raghu KG, Sujathan K, Maiti KK. Elucidating Raman image-guided differential recognition of clinically confirmed grades of cervical exfoliated cells by dual biomarker-appended SERS-tag. *Anal Chem.* 2021;93(32):11140-11150. doi:10.1021/acs.analchem.1c01607 3. Sujai PT, Joseph MM, Saranya G, Nair JB, Murali VP, Maiti KK. Surface charge modulates the internalization vs. penetration of gold nanoparticles: comprehensive scrutiny on monolayer cancer cells, multicellular spheroids and solid tumors by SERS modality. *Nanoscale.* 2020;12(13):6971-6975. doi:10.1039/d0nr00809e 4. Shamjith S, Murali VP, Joesph MM, et al. Hydrogen sulfide-induced activatable photodynamic therapy adjunct to disruption of sub-cellular glycolysis in cancer cells by fluorescence-SERS bimodal iridium metal-organic hybrid. *ACS Appl Mater Interfaces.* 2024;16(21):27114-27126. doi:10.1021/acsami.4c02761. 5. Abraham B, Emmanuel N, Ajikumar N, Sanoop P, Varhese L E, Murali VP et al., A practical nanoplasmonic SERS substrate for differential diagnosis of lung normal and cancer cells through multivariate statistical analysis. *ChemNanoMat.* 2023;7(20):202300378. doi:10.1002/cnma.202300378. Dr. Ashwin Oommen Philips is the medical oncologist and associate professor at Amala institute Medical Sciences with area of specialisation in solid tumour oncology and immune oncology. He has several publications to his credit and he runs several clinical trials and projects. Dr. Ashwin handles the breast cancer patients and DCIS patients. He will be managing the clinical side of this project. Relevant publications 1. Singh Lakhwinder ,Amit S , Ashwin P , Soumya P, Sunu C, et al Unveiling primary platinum resistant ovarian cancer: Demographic and clinical perspectives from multicenter cancer registry in India. *Journal of Clinical Oncology.* 42. e17572. 10.1200/JCO.2024.42.16suppl.e17572. 2. Philips AO, Cyriac S, Unnikrishnan P, et al. "A Multicenter Study on the Challenges and Real-World Utilization of Immune Checkpoint Inhibitors in Resource-Constrained Settings: Insights and Implications from India," *South Asian J Cancer,* 2024;00(00):00-00 3. Mayank K ,Amit S, Ashwin P , Soumya P, Sunu C, Krishnakumar R et al Unveiling the challenges of small cell lung cancer in resource-limited settings: A multicenter collaboration analysis of demographics, treatment modalities, and prognosis. *Journal of Clinical Oncology.* 42. e20103. 10.1200/JCO.2024.42.16suppl.e20103. Dr. Lekha K Nair is a famous pathologist and professor at the Department of Pathology, Amala Institute of Medical sciences. She has immense experience in IHC, Cytopathology, histopathology and molecular pathology fields. She will be monitoring and co-ordinating the immunohistochemical studies of the project and interpreting the results. Relevant publications: 1. Krishnan Nair L, Sankar S. Role of fine needle aspiration cytology in the diagnosis of orbital masses: A study of 41 cases. *J Cytol.* 2014;31(2):87-90. doi:10.4103/0970-9371.138672. 2. Nair LK, Ramakrishnan D, Augustine J. Imprint cytology in bone tumors – A comprehensive 3-year analysis in a tertiary care centre. *GJRA - Global J Res Anal.* 2018;7(4):45-48. Print ISSN No 2277-8160. 3. Palakkan S, Augustine T, Valsan MK, Abdul Vahab KP, Nair LK. Role of frozen section in surgical management of ovarian neoplasm. *Gynecol Minim Invasive Ther.* 2020;9(1):13-17. doi:10.4103/GMIT.GMIT219. 4. Nair LK, Zainudeen F, N S, et al. Comparative study of bronchial brush and bronchial wash cytology in the diagnosis of lung tumors. *J Diagn Pathol Oncol.* 2021;16(1):9-14. doi:10.18231/j.jdpo.2021.003. Dr. Kaustabh Kumar Maiti from CSIR-NIIST is a chemical biologist with extensive experience in the use of Raman spectroscopy for biomedical applications. He has a solid background in organic synthesis, nanoparticle preparation in various sizes and shapes, and a wide range of bio-conjugation techniques. His expertise also includes characterizing materials with advanced analytical instruments such as NMR, HR-MS, LC-MS, HR-TEM, DLS, and Raman imaging, as well as performing computational analysis through molecular modeling. CSIR-NIIST offers interdisciplinary facilities where chemists, material scientists, and biologists collaborate. Dr. Maiti specializes in organic synthesis and the development of nanomaterials for creating nano-biosensors that detect biomarkers, particularly using surface-enhanced Raman spectroscopy (SERS). His work also includes developing nanoparticle probes for biosensors, with a focus on cancer screening. Relevant publications 1. Murali VP, Karunakaran V, Madhukrishnan M, Lekshmi A, Kottarathil S, Deepika S, Saritha VN, Ramya AN, Raghu KG, Sujathan K, Maiti, K. K. A clinically feasible diagnostic spectro-histology built on SERS-nanotags for multiplex detection and grading of breast cancer biomarkers. *Biosensors and Bioelectronics,* 2023, 227, 115177. <https://doi.org/10.1016/j.bios.2023.115177> 2. Karunakaran V, Saritha VN, Joseph MM, et al. Diagnostic spectro-cytology revealing differential recognition of cervical cancer lesions by label-free surface enhanced Raman fingerprints and chemometrics. *Nanomedicine: Nanotechnology, Biology and Medicine.* 2020;9(10):2276. doi:10.1016/j.nano.2020.102276 3. Karunakaran V, Saritha VN, Ramya AN, et al. Elucidating Raman Image-Guided Differential Recognition of clinically confirmed grades of cervical exfoliated cells by dual Biomarker-Appended SERS-TaG. *Analytical Chemistry.* 2021;93(32):11140-11150. doi:10.1021/acs.analchem.1c01607 4. A non-invasive ultrasensitive diagnostic approach for COVID-19 infection using salivary label-free SERS fingerprinting and artificial intelligence Varsha Karunakarana, Manu M.Josepha, InduprabhavYadev, HimanshuSharmac, K.Shamna, Sumeet Saurav, Remanan Pushpa Sreejith, Veena Anand, Rosenara Beegum, S.Reggi David, Thomas lype, K.L.Sarada Devi, A.Nizarudheen, M.S.Sharmad, Rishi Sharma, Ravindra Mukhiya, Eshwar Thouti, Karuvath Yoosaf, Joshy Joseph, P.Sujatha Devi, S.Savithri, Ajay Agarwal, Sanjay Singh, Kaustabh Kumar Maiti *Journal of Photochemistry and Photobiology B: Biology,* 2022, 112545 5. Saranya G, Joseph MM, Karunakaran V, et al. Enzyme-Driven Switchable Fluorescence-SERS diagnostic nanococktail for the multiplex detection of lung cancer biomarkers. *ACS Applied Materials Interfaces.* 2018;10(45):38807-38818. doi:10.1021/acsami.8b15583 Dr. K. V Radhakrishnan is the head and chief scientist at Chemical Sciences and Technology division with expertise in synthetic chemistry. His team can contribute to the Synthesis part of the project. Relevant publications 1. Aswathy, M., Abhijith, B., Lankalapalli, R. S., Radhakrishnan, K. V. (2022). A pentacarbomethoxycyclopentadiene (PCCP) organic Brønsted acid catalyzed stereoselective glycosidation of N-pentenyl orthoesters (NPOE) of d-glucose and d-galactose, in conjunction with N-iodosuccinimide. *Carbohydrate Research,* 522, 108684. <https://doi.org/10.1016/j.carres.2022.108684> 2. Reghukumar C, Shamjith S, Murali VP, et al. Cyclometalated Ir(III) theranostic molecular probe enabled mitochondria-targeted fluorescence-SERS-guided phototherapy in breast cancer cells. *J Photochem Photobiol B Biol.* 2024;250:112832. doi:10.1016/j.jphotobiol.2023.112832. 3. Biji, M., Radhakrishnan, K. V., Lankalapalli, R. S. (2021). Tandem photoisomerization and transannular cyclizations of zerumbone epoxide: a model for Diversity-Oriented synthesis using abundant natural products. *Organic Letters,* 23(15), 5871–5875. <https://doi.org/10.1021/acs.orglett.1c01997>

Institutional Support/ Facilities: As the proposed project is going to a combined organization between clinicians and chemical biology researchers, Amala Institute of Medical Sciences can act as the clinical partner and CSIR-NIIST as the research partner. Amala being one of the renowned cancer hospitals in Kerala with an efficient and well-structured oncology wing can handle the DCIS and IDC patients. The fully equipped and active pathology unit with two automated IHC machines can support the histochemical studies involved in this project. CSIR-NIIST has all the equipment and infrastructure facilities to manage the SERS nanotag synthesis, optimisation and characterization part along with the SERS analysis owing to the experience of Dr. Maiti and Dr. Radhakrishnan in the Nano bioscience and synthetic chemistry fields. Dr. Vishnu Priya Murali being experienced in both IHC and SERS detection modality for biomarker analysis can handle this study by bridging both the partner institutes and can efficiently perform the project execution, study monitoring and data analysis and interpretation. Dr. Ashwin Oommen Philips, being the medical oncologist will handle the clinical side of the project and DCIS and IDC patients Dr. Lekha K Nair, is an experienced pathologist, who can monitor and evaluate the IHC part of the project. Dr. kaustabh Kumar Maiti being a chemical biology scientist with immense knowledge and experience in the field of SERS based biomarker detection and cancer diagnosis, will be managing the SERS based multiplex biomarker detection part of the project Dr. K V Radhakrishnan being a well-known synthetic chemist can monitor the Raman reporter synthesis and characterization part.

Laboratory facilities (in-vitro/ in-silico) Institutional resources such as instruments/ equipment and other physical resources available for use in the project proposed animal house etc. Amala Automated IHC system (Benchmark GX, Roche Diagnostics, USA), Cryostat (Leica). Microtome, HistoCore Arcadia Embedding machine, Tissue processor (Thermo), Real time PCR, Refrigerated centrifuge (Thermo), incubators, Flow cytometer (BD), fluorescent microscope (Leica), conventional PCR, fully equipped cell culture facility, Plate reader, Biosafety cabinet, Laminar air flow chamber, Autoclave, pH meter, Microscope. CSIR-NIIST Confocal Raman Microscope Alpha300R, (WiTEC, Germany), Confocal fluorescent microscope (Zeiss), NMR (Bruker 500 MHz) Avans II, LCMS-MS (Thermo), HPLC (Shimadzu) , Refrigerated High Speed Centrifuge (Heraeus), Thermal Cycler (Veriti, ABI), UV-Vis Spectrophotometer (Shimadzu), Submarine Electrophoresis System (Biotech), Lyophilizer (Martin Christ), Real-Time PCR (ABI), High Speed Tissue Homogenizer (Kinematica), Western Blot Transfer Apparatus Biotech, Chemiluminescence Imaging System FluorChem M, Protein Simple, Liquid Nitrogen Containers IOC, MUSE Cell Analyzer Millipore, -200C Deep Freezer (BlueStar) Genetic Analyzer, Capillary Electrophoresis System Experion,(Biorad), Research Microscope (Leica), Fluorescence Microscope OlympusUV Gel Documentation System GEUltrapur Water System Millipo Laminar Hood BSC, Nuair, CO2 Incubators Nuair, -80 Deep Freezer, Flow Cytometer with Cell Sorter FACSJazz, BD, Manual Sequencing Electrophoresis System Biotech, FISH System Olympus Gradient HPLC System Shimadzu, Spectral Karyotyping (SKY System) Spectra, DLS Horiba, Electrospinning Physics Equipment Co.,Co-PI's Department Magnetic stirrer Hot plate IKA C-MAG HS7, Electronic Balance Shimadzu,High Vacuum pump Hindhiva Direct Drive, ED-6, Lyophilizer Martin Christ, Shaker (bench top) Orbitek L4676 Scigenics Biotech, Inverted Fluorescent Phase contrast microscope Nikon, Model TS-100F, Carbon dioxide Incubator (Eppendorf)

Conflict of Interest declaration (if any) PI has no conflict of interest to declare

Duration (in Months)	36 Months
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Investigator Details

#	Name	Institute	Designation	Email	Contact No.	Nature of Employment	Role in Proposal
1	Dr Vishnu Priya Murali	Amala Institute of Medical Sciences	Scientist C	vishnupriyaem@gmail.com	9895143535	Permanent	PI
2	Dr Kaustabh Kumar Maiti	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Scientist F	kkmaiti@niist.res.in	8547761544	Permanent	Co-PI
3	Dr K.V.Radhakrishnan	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Scientist F	radhu2005@gmail.com	9446555258	Permanent	Co-PI
4	Dr Ashwin Oommen Philips	Amala Institute of Medical Sciences	Associate Professor	drashphilsmog@gmail.com	9003635373	Permanent	Co-PI
5	Dr LEKHA K.NAIR	Amala Institute of Medical Sciences	Professor	lekhamukundan5@gmail.com	9947264644	Permanent	Co-PI

Documents consideration

#	Document Name	Is Applicable?	Uploaded Document	Remarks
1	Declaration & Attestation Form(duly signed by Head of Department/ Director)	Yes	View	Merged PDF with declaration from both Amala Institute of Medical Sciences and CSIR-NIIST
2	Additional supplementary information including figures tables flow diagrams etc can be shared as PDF	Yes	View	Scheme of the proposed project, figures and graphs of previous work done and patent

Proposed Budget Details

Institute	Budget Year	Manpower Budget (Rs.)	Contingency	Consumables	Equipment	Travel	Overhead	Total(Rs)
Amala Institute of Medical Sciences	1	806400.00	50000.00	1000000.00	3500000.00	50000.00	55692	5462092
CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	1	806400.00	50000.00	1000000.00	0	100000.00	55692	2012092
Amala Institute of Medical Sciences	2	806400.00	50000.00	1000000.00	0	50000.00	55692	1962092
CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	2	806400.00	50000.00	1000000.00	0	100000.00	55692	2012092
Amala Institute of Medical Sciences	3	846720.00	50000.00	1000000.00	0	50000.00	55692	2002412
CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	3	846720.00	50000.00	1000000.00	0	100000.00	55692	2052412
Total in (Rs.):		4919040	300000	6000000	3500000	450000	334152	15,503,192.00

Budget Breakup Details (Staff/Manpower)

#	Budget Year	Institute	Designation	No. of Person(nos)	Require Month(nos)	Cost Per Person(Rs.)	Overhead(Rs.)	Total Cost(Rs.)
1	Year: 1	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Project Research Scientist - I (Non Medical)	1	12	67,200	24,192.00	806,400.00
Justification : One project Scientist I non medical is required to perform the SERS nanotag synthesis and characterization, tissue processing and Raman analysis								
2	Year: 1	Amala Institute of Medical Sciences	Project Research Scientist - I (Non Medical)	1	12	67,200	24,192.00	806,400.00
Justification : One project Scientist I non medical is required to perform and monitor the sample collection, IHC and data analysis								
3	Year: 2	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Project Research Scientist - I (Non Medical)	1	12	67,200	24,192.00	806,400.00
Justification : One project Scientist I non medical is required to perform the SERS nanotag synthesis and characterization, tissue processing and Raman analysis								
4	Year: 2	Amala Institute of Medical Sciences	Project Research Scientist - I (Non Medical)	1	12	67,200	24,192.00	806,400.00
Justification : One project Scientist I non medical is required to perform IHC screening for biomarkers and data analysis								
5	Year: 3	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Project Research Scientist - I (Non Medical)	1	12	70,560	24,192.00	846,720.00
Justification : One project Scientist I non medical is required to perform the SERS nanotag synthesis and characterization, tissue processing and Raman analysis								
6	Year: 3	Amala Institute of Medical Sciences	Project Research Scientist - I (Non Medical)	1	12	70,560	24,192.00	846,720.00
Total Cost (Rs.) including overhead								5,064,192.00

Budget Breakup Details (Staff/Manpower)**Justification** :One project Scientist I non medical is required to perform IHC screening for biomarkers and data analysis**Total Cost (Rs.)**

including overhead

5,064,192.00**Contingency budget breakup details**

#	Budget Year	Institute	Overhead Charges (Rs.)	Total Cost(Rs.)
1	Year: 1	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	1,500.00	50,000.00
Contingency Name :Printing / DTP and others: 15000.00 Report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :A contingency of Rs. 50000 per year is essential to meet the printing charges, to meet unforeseen expenses and also to attend seminars and conferences etc				
2	Year: 1	Amala Institute of Medical Sciences	1,500.00	50,000.00
Contingency Name :Computer accessories/hard disk : 15000.00 Report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :Rs. 50000 per year is required as the contingency amount towards the printing, report preparation and also for computer accessories procurement				
3	Year: 2	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	1,500.00	50,000.00
Contingency Name :Printing / DTP and others: 15000.00 Report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :A contingency of Rs. 50000 per year is essential to meet the printing charges, to meet unforeseen expenses and also to attend seminars and conferences etc				
4	Year: 2	Amala Institute of Medical Sciences	1,500.00	50,000.00
Contingency Name :Printing / DTP and others: 15000.00 Report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :Rs. 50000 per year is required as the contingency amount towards the printing, report preparation and also to attend conferences				
5	Year: 3	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	1,500.00	50,000.00
Contingency Name :Printing / DTP and others: 15000.00 report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :A contingency of Rs. 50000 per year is essential to meet the printing charges, to meet unforeseen expenses and also to attend seminars and conferences etc				
6	Year: 3	Amala Institute of Medical Sciences	1,500.00	50,000.00
Contingency Name :Printing / DTP and others: 15000.00 Report preparation unforeseen expenses : 10000.00 Attending seminar/consortium : 25000.00				
Justification :Rs. 50000 per year is required as contingency to meet the printing charges, for attending conferences, to meet unforeseen expenses etc				
Total Cost (Rs.)				309,000.00
including overhead				

Consumables Budget Breakup Details

#	Budget Year	Institute	Consumables Name	Overhead	Total Cost(Rs.)
1	Year: 1	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential for the smooth running of the project					
Total Cost (Rs.)					6,180,000.00
including overhead					

Consumables Budget Breakup Details

2	Year: 1	Amala Institute of Medical Sciences	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential for the smooth running of the project					
3	Year: 2	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential for the smooth running of the project					
4	Year: 2	Amala Institute of Medical Sciences	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential for the smooth running of the project					
5	Year: 3	CSIR-National Institute For Interdisciplinary Science and Technology(CSIR-NIIST)	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential to execute the project works					
6	Year: 3	Amala Institute of Medical Sciences	Antibodies – 700000.00 Chemicals - 100000.00 Reagents kits – 100000.00 Other consumables- 100000.00	30,000.00	1,000,000.00
Justification : Consumables like antibodies, reagents, chemicals, kits, plastic wares and other consumables are very much essential to execute the project works					
Total Cost (Rs.) including overhead					6,180,000.00

Equipment Budget Breakup Details

#	Budget Year	Institute	Equipment Name	Equipment Model	Equipment Manufacturer	Equipment Type	Total Cost(Rs.)
1	Year: 1	Amala Institute of Medical Sciences	Small laboratory equipments like shaker, fridge, vortex, pH meter etc			Domestic	100,000.00
Justification : These small equipment's are required for the buffer and reagent preparation , storage etc							
Mode of Proposed disposal : Institute handover							
2	Year: 1	Amala Institute of Medical Sciences	PAGE and Western blot apparatus with power pack power supply	Mini PROTEAN Tetra Cell and Mini transblot module	Biorad	Imported	400,000.00
Justification : It is required for the parallel confirmation of the biomarker expression profile through westernblot analysis							
Mode of Proposed disposal : Institute handover							
3	Year: 1	Amala Institute of Medical Sciences	-80 deep freezer	CryoCube® F440n	Eppendorf	Imported	1,000,000.00
Justification :- 80 deep-freezer is very much essential to store antibodies, protein and RNA samples which will be used for the parellel confirmations							
Mode of Proposed disposal : Institute handover							
4	Year: 1	Amala Institute of Medical Sciences	Inverted Fluorescence and Phase contrast Cell Tissue culture microscope	EVIDENT OLYMPUS CKX 53 with DP23M Monochrome Camera	Olympus	Imported	2,000,000.00
Total (Rs.):							3,500,000.00

Equipment Budget Breakup Details

Justification :It is required to take the images of tissue samples, IHC and FISH for manuscript and report preparation and also to produce supporting data using cultured cells for publication purpose

Mode of Proposed disposal :Institute handover

Total (Rs.): 3,500,000.00

Travel Justification

#	Year	Amount(Rs.)
1	Year: 1	100000.00
Justification : This is needed for sample collection, to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
2	Year: 1	50000.00
Justification : This is needed to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
3	Year: 2	100000.00
Justification : This is needed for sample collection, to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
4	Year: 2	50000.00
Justification : This is needed to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
5	Year: 3	100000.00
Justification : This is needed for sample collection, to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
6	Year: 3	50000.00
Justification : This is needed to attend review meetings by the investigators and conferences, seminars, symposia and training courses for the investigators and project personnel		
Total:		450,000.00

Short resume PI/Co-PI

Name of PI/Co-Pi	DOB	Domain Expertise	Number of articles in Pub Med (Past 10 years)	h-index	Fellow of Academies	Role in Proposal
Dr Ashwin Oommen Philips	1982-10-23	Medical Oncology- Solid Tumor oncology	5	3	Member- ISMPO, AMPOK, ESMO, ASCO	Co-PI

Short resume PI/Co-PI

Maximum of 10 primary research publications related to the proposal

Publication details in AMA style	Impact factor of journal	Author type (first, corresponding, coauthor)	Name of policy/programme/ protocol document or patent/commercialization of products where cited.
Philips, Ashwin O Kaur, Tejinder Garg, Shirin Sharma, Ishu Anand, Mridul Batta, Nishant Singh, Harpreet. Clinical profile and outcomes of patients with endometrial cancer from Northwest India: A retrospective study. Cancer Research, Statistics and Treatment 7(4):p 403-409, Oct–Dec 2024. DOI: 10.4103/crst.crst4024	0	Corresponding and First author	NA
Mayank K ,Amit S, Ashwin P , Soumya P, Sunu C, Krishnakumar R et al Unveiling the challenges of small cell lung cancer in resource-limited settings: A multicenter collaboration analysis of demographics, treatment modalities, and prognosis. Journal of Clinical Oncology. 42. e20103. 10.1200/JCO.2024.42.16suppl.e20103.	42.1	Co-author	NA
Singh Lakhwinder ,Amit S , Ashwin P , Soumya P, Sunu C, et al Unveiling primary platinum resistant ovarian cancer: Demographic and clinical perspectives from multicenter cancer registry in India. Journal of Clinical Oncology. 42. e17572. 10.1200/JCO.2024.42.16suppl.e17572.	42.1	Co-author	NA
Philips AO, Cyriac S, Unnikrishnan P, et al. "A Multicenter Study on the Challenges and Real-World Utilization of Immune Checkpoint Inhibitors in Resource-Constrained Settings: Insights and Implications from India," South Asian J Cancer, 202400(00):00-00	0.6	Corresponding and First author	NA
Philips A, Soumya P, Sunu C, Moharana, et al. "Real-World Experiences of Next-Generation Sequencing in Oncology: From an Indian Multicenter Registry and Collaborative Centers," Indian Journal of Medical and Paediatric Oncology. DOI: 10.1055/s-0044-1779275.	0.3	Corresponding and First author	NA
Mall A, Negi P, Philips AO, Kingsley PA. "Induction chemotherapy in head and neck cancers – Boon or bane" J Can Res Ther, 202319:420-5.	1.3	Co-author	NA

Experience as Investigator (completed projects)

Title of the project	Role	Funding Agency	Amount of Funding	Reference of main publications
Network Of Oncology Clinical Trials In India, NOCI	PI	BIRAC	95800000.00	Under preparation

All Ongoing research projects

Project Id	Title	Grant Amount	Funding Agency	Start Date	End Date	Duration
NHRP-2023-0001870	A multicentric noninferiority trial to compare sublingual Buprenorphine versus oral Tramadol for cancer pain	20000000.00	ICMR	2024-04-23	2027-04-22	36
Not available	Total Neoadjuvant Therapy in High-Risk Locally Advanced Rectal Cancer:Multicentric Observational Study in the Indian Population (TIDE-R Study)	0.00	investigator initiated	2024-04-01	2029-03-31	60

Name of PI/Co-Pi	DOB	Domain Expertise	Number of articles in Pub Med (Past 10 years)	h-index	Fellow of Academies	Role in Proposal
Dr LEKHA K.NAIR	1976-05-15	• Cytopathology • Histopathology • Molecular pathology	7	3	• Indian Medical Association • Indian Association of Pathologists and Microbiologists • Indian Association of Cytologists • Fellow of Royal College of Pathologists, UK	Co-PI

Short resume PI/Co-PI

Maximum of 10 primary research publications related to the proposal

Publication details in AMA style	Impact factor of journal	Author type (first, corresponding, coauthor)	Name of policy/programme/ protocol document or patent/commercialization of products where cited.
Nair LK, Zainudeen F, N S, et al. Comparative study of bronchial brush and bronchial wash cytology in the diagnosis of lung tumors. J Diagn Pathol Oncol. 20216(1):9-14. doi:10.18231/jjdpo.2021.003.	0	First	NA
K Nair L Das A Kumar A S A Ramachandran V. Self Regressing Epitheloid Haemangioendothelioma of Tibia in an Infant-A rare case report and review of literature. J. orthop. case rep. 2015 5(1):37-40. doi: 10.13107/jocr.2250-0685.251	1.91	First	NA
Mansoor CA, Bhargavan PV, Rajanish R, Nair LR. Disseminated histoplasmosis. Indian J Orthop. 201347:639-642. doi:10.4103/0019-5413.121601.	0.3	Co-author	NA
Palakkan S, Augustine T, Valsan MK, Abdul Vahab KP, Nair LK. Role of frozen section in surgical management of ovarian neoplasm. Gynecol Minim Invasive Ther. 20209(1):13-17. doi:10.4103/GMIT.GMIT219.	1.4	Corresponding	NA
Abdulla MC, Alungal J, Nair LK, Musambil M. Malignancy-associated microangiopathic hemolytic anemia and thrombocytopenia. Indian J Med Paediatr Oncol. 201839(2):254-256. doi:10.4103/ijmpo.ijmpo12816.	0.3	Co-author	NA
Nair LK, Ramakrishnan D, Augustine J. Imprint cytology in bone tumors – A comprehensive 3-year analysis in a tertiary care centre. GJRA - Global J Res Anal. 20187(4):45-48. Print ISSN No 2277-8160.	0.978	First author	NA
Krishnan Nair L, Sankar S. Role of fine needle aspiration cytology in the diagnosis of orbital masses: A study of 41 cases. J Cytol. 201431(2):87-90. doi:10.4103/0970-9371.138672.	1	First	NA

Experience as Investigator (completed projects)

Title of the project	Role	Funding Agency	Amount of Funding	Reference of main publications
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All Ongoing research projects

Project Id	Title	Grant Amount	Funding Agency	Start Date	End Date	Duration
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Name of PI/Co-Pi	DOB	Domain Expertise	Number of articles in Pub Med (Past 10 years)	h-index	Fellow of Academies	Role in Proposal
Dr K.V.Radhakrishnan	1969-05-21	Multi-step Organic Synthesis, Methodology Development, Bio-prospecting of medicinal plants, Synthetic carbohydrate chemistry, Phytochemistry, Ayurvedic Drug Development Process Chemistry for APIs	79	28	NA	Co-PI

Short resume PI/Co-PI

Maximum of 10 primary research publications related to the proposal

Publication details in AMA style	Impact factor of journal	Author type (first, corresponding, coauthor)	Name of policy/programme/ protocol document or patent/commercialization of products where cited.
Biji, M., Radhakrishnan, K. V., Lankalapalli, R. S. (2021). Tandem photoisomerization and transannular cyclizations of zerumbone epoxide: a model for Diversity-Oriented synthesis using abundant natural products. <i>Organic Letters</i> , 23(15), 5871–5875. https://doi.org/10.1021/acs.orglett.1c01997	6	Corresponding	CSIR
Krishnapriya, Sasikumar, P., Aswathy, M., Prem, P. T., Radhakrishnan, K. V., Chakrapani, P. S. B. (2022). Plant derived bioactive compounds and their potential to enhance adult neurogenesis. <i>Phytomedicine Plus</i> , 2(1), 100191. https://doi.org/10.1016/j.phyplu.2021.100191	2.4	Corresponding	CSIR
Subramanyan, S., Karunakaran, V., Deepika, S., Gracy, A. J., Veluthoor, S., Joseph, K. H., Maiti, K. K., Varma, R. L., Radhakrishnan, K. V. (2022). Libocedroquinone: A Promising Anticancer Lead against Lung Cancer from <i>Calocedrus Decurrens</i> . <i>Planta Medica International Open</i> , 9(01), e54–e59. https://doi.org/10.1055/a-1699-8748	2.7	Corresponding	CSIR
Biji, M., Prabha, B., Lankalapalli, R. S., Radhakrishnan, K. V. (2021). Transition Metal/Lewis Acid Catalyzed Reactions of Zerumbone for Diverse Molecular Motifs. <i>The Chemical Records</i> , 21(12), 3943–3953. https://doi.org/10.1002/tcr.202100206	6.7	Corresponding	CSIR
Pothiyil SV, Sivadas N, Murali VP, et al. Exploring apoptotic induction of malabaricone A in triple-negative breast cancer cells: an acylphenol phyto-entity isolated from the fruit rind of <i>Myristica malabarica</i> Lam. <i>RSC Med Chem</i> . 202415:3558-3575. doi:10.1039/D4MD00	4.1	Corresponding	CSIR
Reghukumar C, Shamjith S, Murali VP, et al. Cyclometalated Ir(III) theranostic molecular probe enabled mitochondria-targeted fluorescence-SERS-guided phototherapy in breast cancer cells. <i>J Photochem Photobiol B Biol</i> . 2024250:112832. doi:10.1016/j.jphotobiol.2023.112832.	5.4	Corresponding	ICMR and CSIR funded
Meenu, M. T., Kaul, G., Akhir, A., Shukla, M., Radhakrishnan, K. V., Chopra, S. (2022). Developing the Natural Prenylflavone Artocarpin from <i>Artocarpus hirsutus</i> as a Potential Lead Targeting Pathogenic, Multidrug-Resistant <i>Staphylococcus aureus</i> , Persisters and Biofilms with No Detectable Resistance. <i>Journal of Natural Products</i> , 85(10), 2413–2423. https://doi.org/10.1021/acs.jnatprod.2c00621	4.8	Corresponding	CSIR
Anish, R. J., Mohanan, B., Aswathy, T. R., Nair, A. K., Radhakrishnan, K., Rauf, A. A. (2023). An integrated approach to the structural characterization, long-term toxicological and anti-inflammatory evaluation of <i>Pterospermum rubiginosum</i> bark extract. <i>Journal of Ethnopharmacology</i> , 308, 116262. https://doi.org/10.1016/j.jep.2023.116262	5.08	Corresponding	CSIR
Valsan, A., Meenu, M. T., Murali, V. P., Malgija, B., Joseph, A. G., Nisha, P., Radhakrishnan, K. V., and Maiti, K. K. (2023). Exploration of Phaeanthine: Abisbenzylisoquinoline alkaloid induces anticancer effect in cervical cancer cells involving Mitochondria-Mediated apoptosis. <i>ACS Omega</i> . https://doi.org/10.1021/acsomega.3c01023	4.13	Corresponding	CSIR
Aswathy, M., Abhijith, B., Lankalapalli, R. S., Radhakrishnan, K. V. (2022). A pentacarbomethoxycyclopentadiene (PCCP) organic Brønsted acid catalyzed stereoselective glycosidation of N-pentenyl orthoesters (NPOE) of d-glucose and d-galactose, in conjunction with N-iodosuccinimide. <i>Carbohydrate Research</i> , 522, 108684. https://doi.org/10.1016/j.carres.2022.108684	2.97	Corresponding	CSIR

Experience as Investigator (completed projects)

Title of the project	Role	Funding Agency	Amount of Funding	Reference of main publications
Early detection of multiple cancers from blood plasma by surface enhanced Raman scattering (SERS) and Artificial intelligence	Co-PI	TATA ELXSI LTD	8800000.00	Applied for patent
Transition Metal/Lewis Acid Mediated Reactions of Strained Diazanorbornenes and Carbonyl Compounds: Efficient Access to Biologically Relevant Scaffolds".	PI	SERB/Department of Science and Technology	5300000.00	Completed

Short resume PI/Co-PI

All Ongoing research projects

Project Id	Title	Grant Amount	Funding Agency	Start Date	End Date	Duration
CRG/2023/000630	Design, Synthesis of Novel Naphthalene-Bipyridine appended Iridium (Nap-Ir) Photosensitiser for Targeted Nanoparticle Based Phototherapy in Breast Cancer Modelquot.	5800000.00	SERB	2024-04-01	2027-03-31	36
2020-9597	Diagnostic Evaluation of a SERS-Nanoprobe Based Immunosensor for Early Detection of Alzheimer's Disease Biomarkers from Blood	10298000.00	ICMR	2022-03-29	2025-03-28	36
EM/IG/Dev.Res/2023-0001476	Development of Spectro-Cytology Screening Technology for Detection of Grades of Cervical Cancer Lesions by Surface Enhanced Raman Spectroscopy (SERS) and Artificial Intelligence	39600000.00	ICMR	2024-03-01	2028-02-29	48

Name of PI/Co-Pi	DOB	Domain Expertise	Number of articles in Pub Med (Past 10 years)	h-index	Fellow of Academies	Role in Proposal
Dr Kaustabh Kumar Maiti	1969-10-23	i) Nano bioscience: Utilization of Surface-Enhanced Raman Spectroscopy (SERS) ii) Ultrasensitive detection of human cancers by SERS-nanoprobes and AI iii) Multimodal targeted theranostic nano-constructs for cancer treatment iv) In-vitro cell-based assays for HIT/Advanced HITs for anti-cancer profiling v) Metabolic Glycan Labelling (MGL) by Raman imaging	70	32	NA	Co-PI

Short resume PI/Co-PI

Maximum of 10 primary research publications related to the proposal

Publication details in AMA style	Impact factor of journal	Author type (first, corresponding, coauthor)	Name of policy/programme/ protocol document or patent/commercialization of products where cited.
New Insight of Tetraphenylethylene-based Raman Signatures for Targeted SERS Nanoprobe Construction Toward Prostate Cancer Cell Detection Adukkadan N. Ramya, Manu M. Joseph, Jyothi B. Nair, Varsha Karunakaran, Nisha Narayanan, and Kaustabh Kumar Maiti, ACS Appl. Mater. Interfaces., 2016, 8, 10220-10225	9.5	Corresponding	CSIR healthcare Theme
Sujai PT, Shamjith S, Joseph MM, Maiti KK. Elucidating Gold–MnO ₂ Core–Shell Nanoenvelope for Real Time SERS-Guided Photothermal Therapy on Pancreatic Cancer Cells. ACS Applied Bio Materials. 2021;4(6):4962-4972. doi:10.1021/acsabm.1c00241	4.8	Corresponding	CSIR healthcare Theme
Joseph MM, Ramya AN, Vijayan VM, et al. Targeted Theranostic Nano Vehicle Endorsed with Self-Destruction and Immunostimulatory Features to Circumvent Drug Resistance and Wipe-Out Tumor Reinitiating Cancer Stem Cells. Small. 2020;16(38):2003309. doi:10.1002/sml.202003309	15.15	Corresponding	CSIR Healthcare theme and SERB support
An Efficient Molecular Luminophore based on Tetraphenylethylene (TPE) Enabling intracellular Detection and Therapeutic Benefits of Hydrogen Sulfide in Alzheimer's Disease Adukkadan N. Ramya, Manu M. Joseph, Varsha Karunakaran, Chekrain Valappil Shihash Ahammed, Animesh Samanta, Kaustabh K. Maiti Sensors and Actuators B: Chemical, 355 (2022), 131118	9.22	Corresponding	CSIR healthcare theme and CSIR support
Sujai PT, Joseph MM, Saranya G, Nair JB, Murali VP, Maiti KK. Surface charge modulates the internalization vs. penetration of gold nanoparticles: comprehensive scrutiny on monolayer cancer cells, multicellular spheroids and solid tumors by SERS modality. Nanoscale. 2020;12(13):6971-6975. doi:10.1039/d0nr00809e	8	Corresponding	CSIR Healthcare theme and DBT support
Saranya G, Joseph MM, Karunakaran V, et al. Enzyme-Driven Switchable Fluorescence-SERS diagnostic nanococktail for the multiplex detection of lung cancer biomarkers. ACS Applied Materials Interfaces. 2018;10(45):38807-38818. doi:10.1021/acsami.8b15583	9.5	Corresponding	CSIR Healthcare theme , DST SERB support
A non-invasive ultrasensitive diagnostic approach for COVID-19 infection using salivary label-free SERS fingerprinting and artificial intelligence Varsha Karunakarana, Manu M. Josepha, Induprabhav Yadev, Himanshu Sharmac, K. Shamna, Sumeet Saurav, Remanan Pushpa Sreejith, Veena Anand, Rosenara Beegum, S. Regi David, Thomas Iype, K.L. Sarada Devi, A. Nizarudheen, M.S. Sharmad, Rishi Sharma, Ravindra Mukhiya, Eshwar Thouti, Karuvath Yoosaf, Joshy Joseph, P. Sujatha Devi, S. Savithri, Ajay Agarwal, Sanjay Singh, Kaustabh Kumar Maiti Journal of Photochemistry and Photobiology B: Biology, 2022, 112545	6	Corresponding	CSIR Healthcare theme , DBT support
Karunakaran V, Saritha VN, Joseph MM, et al. Diagnostic spectro-cytology revealing differential recognition of cervical cancer lesions by label-free surface enhanced Raman fingerprints and chemometrics. Nanomedicine: Nanotechnology, Biology and Medicine. 2020;12(10):202276. doi:10.1016/j.nano.2020.102276	6.45	Corresponding	CSIR, Healthcare theme (12th FYP) Project: M2D Patent filed Indian Patent Appl. No. 201811028087 Dated : 26-07-2018 PCT Int. Appl. (2020), WO 2020021568 A1 20200130. Language: English, Database: CAPLUS, Date: 30th January, 2020
Karunakaran V, Saritha VN, Ramya AN, et al. Elucidating Raman Image-Guided Differential Recognition of clinically confirmed grades of cervical exfoliated cells by dual Biomarker-Appended SERS-TaG. Analytical Chemistry. 2021;93(32):11140-11150. doi:10.1021/acs.analchem.1c01607	8	Corresponding	CSIR, Healthcare theme (12th FYP)
Murali VP, Karunakaran V, Madhukrishnan M, Lekshmi A, Kottarathil S, Deepika S, Saritha VN, Ramya AN, Raghu KG, Sujathan K, Maiti, K. K. A clinically feasible diagnostic spectro-histology built on SERS-nanotags for multiplex detection and grading of breast cancer biomarkers. Biosensors and Bioelectronics, 2023, 227, 115177. https://doi.org/10.1016/j.bios.2023.115177	10.7	Corresponding	CSIR Mission Mode Project (HCP 0012) under healthcare theme DST Nano Mission Patent filed Application No. PCT/IN2021/050577, dated 14-06-2021

Short resume PI/Co-PI

Experience as Investigator (completed projects)

Title of the project	Role	Funding Agency	Amount of Funding	Reference of main publications
Development of an Ultrasensitive, Rapid and Portable system for COVID-19 screening using Label-free Raman Fingerprinting and AI	PI	CSIR	1200000.00	https://doi.org/10.1016/j.jphotobiol.2022.112545
Nanobiosensors and Microfluidics for Healthcare - Development of SERS-Nanoprobe for Multiplexing Diagnosis of Breast and Lung Cancer Biomarkers in Tumor Tissue Samples By Raman Fingerprint	PI	CSIR	74000000.00	https://doi.org/10.1016/j.bios.2023.115177
Natural Products as Affordable Healthcare Agents (NaPaHa) - Isolation Of Anticancer Agent From Hydnocarpus Wightiana Blume and Its Semi-Synthetic Modifications For Enhanced Anticancer Activity	PI	CSIR	41300000.00	DOI: 10.1039/c6ra08724h
Nanomaterials: Application and Impact On Safety, Health And Environment (NanoSHE) - Gold Nanorod based Theranostic Nanoprobe for Phothermal Chemotherapy to MMP2 expressed cancer tumors	PI	CSIR	11600000.00	doi:10.1021/acsami.8b15583
Molecules To Materials To Devices (M2D) - Probes for SERS-based detection of cervical cancer	PI	CSIR	83100000.00	doi:10.1016/j.nano.2020.102276, doi:10.1021/acsami.7b03191
Development Of Multiplexing Detection Platform Of Breast Cancer Biomarkers By Non-Invasive Surface Enhanced Raman Scattering (SERS) Nanoprobe	PI	DST nano mission	3720000.00	https://doi.org/10.1016/j.bios.2023.115177 http://doi:10.1039/d0nr00809e
Biocompatible Combined Polymer-Polysaccharide Core-shell VEGF-Targeted Nano-Carrier For Sustained Intraocular Pharmacotherapy Towards Diabetic Retinopathy	PI	DBT	5123000.00	Manuscript under preparation
Gold Nanorod Based Targeted Nanoprobe For Cancer Theranostics: Diagnosis By Surface Enhanced Raman Scattering (Sers) And Fluorescence Imaging And Therapy By PDTand PTT	PI	DBT	8422400.00	https://doi.org/10.1039/c6nr03385g https://doi.org/10.1021/acs.jpcc.1c08609

All Ongoing research projects

Project Id	Title	Grant Amount	Funding Agency	Start Date	End Date	Duration
2020-9597	DIAGNOSTIC EVALUATION OF A SERS-NANOPROBE BASED IMMUNOSENSOR FOR EARLY DETECTION OF ALZHEIMER'S DISEASE BIOMARKERS FROM BLOOD	10298000.00	ICMR	2022-03-29	2025-03-28	36
IIRPIG-2023-0001476/F1	Development of Spectro-Cytology Screening Technology for Detection of Grades of Cervical Cancer Lesions by Surface Enhanced Raman Spectroscopy (SERS) and Artificial Intelligence	34600000.00	ICMR	2024-03-01	2028-02-29	48

Name of PI/Co-Pi	DOB	Domain Expertise	Number of articles in Pub Med (Past 10 years)	h-index	Fellow of Academies	Role in Proposal
Dr Vishnu Priya Murali	1987-01-30	• Biomarker analysis in solid and liquid samples • Immunohistochemistry, immune assays and omics studies for biomarker analysis • SERS based diagnostic platform • Immunotherapy and targeted nanodelivery systems • In vitro and in vivo anti-cancer studies	20	12	Nil	PI

Short resume PI/Co-PI

Maximum of 10 primary research publications related to the proposal

Publication details in AMA style	Impact factor of journal	Author type (first, corresponding, coauthor)	Name of policy/programme/ protocol document or patent/commercialization of products where cited.
Shamjith S, Joseph MM, Murali VP, et al. NADH-depletion triggered energy shutting with cyclometalated iridium (III) complex enabled bimodal luminescence-SERS sensing and photodynamic therapy. Biosens Bioelectron. 2022;204:114087. doi:10.1016/j.bios.2022.114087.	10.7	Co-author	CSIR, UGC and DHR assisted
Maiti M, Murali VP, Deepika S, Podder A, Maiti KK, Bhuniya S. NADH-induced "kick-on" fluorescent probe validates crosstalk with redox regulator GSH. Sens Actuators B Chem. 2019;299:126964. doi:10.1016/j.snb.2019.126964.	8.4	Equal authorship-First author	CSIR
Podder A, Murali VP, Deepika S, Dhamija A, Biswas S, Maiti KK, Bhuniya S. NADH-activated dual-channel fluorescent probe for multicolor labeling of live cells and tumor mimic spheroid. Anal Chem. 2020;92(18):12356-12362. doi:10.1021/acs.analchem.0c02049	8	Equal authorship-First author	CSIR
Abraham B, Emmanuel N, Ajikumar N, Sanoop P, Varhese L E, Murali VP et al., A practical nanoplasmonic SERS substrate for differential diagnosis of lung normal and cancer cells through multivariate statistical analysis. ChemNanoMat. 2023;e202300378. doi:10.1002/cnma.202300378.	3.1	Co-author	CSIR - FTT
Shamjith S, Murali VP, Joesph MM, et al. Hydrogen sulfide-induced activatable photodynamic therapy adjunct to disruption of sub-cellular glycolysis in cancer cells by fluorescence-SERS bimodal iridium metal-organic hybrid. ACS Appl Mater Interfaces. 2024;16(21):27114-27126. doi:10.1021/acsami.4c02761.	9.5	Co-author	DHR-ICMR support
Murali VP, Kuttan G. Curculigoside augments cell-mediated immune responses in metastatic tumor-bearing animals. Immunopharmacol Immunotoxicol. 2016;15(2):205-215. doi:10.1080/08923973.2016.1188401.	1.2	First	DST INSPIRE
Biswas S, Sarkar S, Dhamija A, Murali VP, Maiti KK, Bhuniya S. Monitoring glutathione dynamics in DNA replication (S-phase) using a two-photon reversible ratiometric fluorescent probe. J Mater Chem B. 2023;11:1948. doi:10.1039/d2tb02231a.	7.4	Corresponding	DHR-ICMR support
Sujai PT, Joseph MM, Saranya G, Nair JB, Murali VP, Maiti KK. Surface charge modulates the internalization vs. penetration of gold nanoparticles: comprehensive scrutiny on monolayer cancer cells, multicellular spheroids and solid tumors by SERS modality. Nanoscale. 2020;12(13):6971-6975. doi:10.1039/d0nr00809e	8	Co-author	CSIR Mission Mode Project
Karunakaran V, Saritha VN, Ramya AN, Murali VP, Raghu KG, Sujathan K, Maiti KK. Elucidating Raman image-guided differential recognition of clinically confirmed grades of cervical exfoliated cells by dual biomarker-appended SERS-tag. Anal Chem. 2021;93(32):11140, 11150. doi:10.1021/acs.analchem.1c01607	8	Co-author	ICMR and CSIR funded
Murali VP, Karunakaran V, Murali M, et al. A clinically feasible diagnostic spectro-histology built on SERS-nanotags for multiplex detection and grading of breast cancer biomarkers. Biosens Bioelectron. 2023;227:115177. doi:10.1016/j.bios.2023.115177.	10.7	First	CSIR Mission Mode Project (HCP 0012) under healthcare theme, DHR, DST Patent filed Application No. PCT/IN2021/050577, dated 14-06-2021

Experience as Investigator (completed projects)

Title of the project	Role	Funding Agency	Amount of Funding	Reference of main publications
Development Of A Sandwich Model Magnetic Capture System For The Detection Of Pancreatic Cancer Biomarkers In Serum By SERS Based Immune Assay	PI	DHR	4485650.00	Vishnu Priya Murali, Shanmughan Shamjith, Thomas P K, Kaustabh Kumar Maiti. A SERS based immune assay for the differential diagnosis of pancreatic cancer biomarkers in plasma samples. Manuscript under preparation, https://doi.org/10.1039/D4MD00318G , https://doi.org/10.1021/acsami.4c02761 , DOI: 10.1039/d2tb02231a

Short resume PI/Co-PI

All Ongoing research projects

Project Id	Title	Grant Amount	Funding Agency	Start Date	End Date	Duration
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Declaration

I hereby declare that the entries in this form and the additional particulars, if any, furnished herewith are true to the best of my knowledge and belief. I understand that in the event of my information being found false or incorrect at any stage, my project/proposal shall be liable to cancellation / termination without notice or any compensation in lieu thereof.

I hereby certify that the research proposal I have submitted to ICMR, New Delhi, for potential funding is entirely my original idea and has not been copied or replicated from any other source. Furthermore, I confirm that this proposal has undergone scrutiny using a standard plagiarism detection tool, verifying its originality and confirming that its contents have not been directly taken from any other sources. Additionally, I declare that there have been no established or pending plagiarism charges against me in the last five years.

In the event that the funding agency identifies any form of plagiarism or inconsistencies in the aforementioned proposal, I acknowledge and agree to comply with any actions deemed necessary by ICMR. I take full responsibility for any such discrepancies and will adhere to the consequences as required.