

Indian Science Technology and Engineering facilities Map (I-STEM)

Invites application for

1. Partial financial support for using R&D facilities in other institutions through the I-STEM web portal to Users from Academic Institutions and Start-ups (Format-1)

Format for requesting support for accessing and using facilities through the I-STEM web portal.

(i) Details of the Personal Information

- a. Name of the Researcher/Faculty Member: Varnitha M
- b. Name of Supervisor: Dr. I.V.Muthuvijayan Enoch
- c. Name of the Institution/Start-up: Karunya Institute of Technology and Sciences, Coimbatore, Tamilnadu.
- d. Name of the Department: Center for Nanoscience and Genomics
- e. Degree registered for/Product being developed (for start-up): Ph.D
- f. Mob. No. 8248643841
- g. Email ID: varnithanair26@gmail.com

(ii) Project/Research topic Details: Separate page attached

- a. Project Title/Research Title: NIR Responsive Magnetic Nanoparticles for Photochemothermal therapy
- b. Sub area: Cancer Nanomedicine

c. Area Description: The project proposal originates from the following pertinence: breast cancer is one of the leading causes of death due to cancer in India (projected to reach 150,000 cases in 2025); to put brakes on the alarming rise of cancer patients, newer strategies in the treatment of the disease are essential. A technique that has recently gained wide attention is photothermal therapy (PTT) employing laser irradiation leading to the ablation of tumor cells. It occurs due to the incorporation of Near-Infrared (NIR) absorption in the tumor cells and allows the heating of cancer cells by laser absorption. Breast cancer possessing destructive lesions and poorly defined margins is difficult to deal with. The poor definition of margin makes them difficult to cure with surgical procedures. To overcome this threatening disease, a multi-modal approach is an essential need focused on the cure of the disease. Although there are reports on several nanomaterials that absorb light in the NIR window I (630–950 nm), the design and synthesis of nanomaterials that absorb in the window II (1000–1600 nm), are finger-countable. In principle, effective NIR II-absorbing nanomaterials should allow deeper penetration of radiation and employ low power in the treatment of breast cancer. At this crucial moment of nanoparticle-based photothermal therapy gaining attention as a promising treatment method, functional nanomaterials possessing the ability to effectively absorb radiation in the NIR window II and show significant photothermal heating efficiency are required. To be more specific, the most commonly utilized 808 nm laser irradiation can be replaced with excitation at 1064 nm. It necessitates the development of new and efficient NIR-II absorbing nanomaterials. In addition, photothermal heating triggers the release of anticancer drugs loaded on their surface. It allows a combined photothermal and chemotherapy. Therefore, the proposal emerges from the perspective of developing novel 1064 nm-excitable nanoscale PTT agents that possess an enhanced anticancer drug-loadable surface, and luminescence property that enables them visible under a fluorescence microscope.

A thorough screening of the literature reveals a gap in the following aspects: 1. Relatively, there are few reports on the application of 1064 nm laser for PTT both in vitro and in vivo (all of the reports were published within the past 4 years. Notwithstanding these, materials showing sharp and strong absorption bands above 1000 nm, almost have not been utilized for PT heating. Instead, the red-edge absorption

or the residual absorption is utilized. Further, all of the work reported employs high power densities. It is to be noted that the skin tolerance is 0.8 Wcm^{-2} . A strategic design of nanomaterials is needed. It can be achieved by designing and synthesizing sulfides of rare earth viz., Nd and Dy and tuning them for effective and safe PTT, proposed herein. 2. At the national level, albeit less in the count, commendable work has been carried out on PTT in the NIR I region. Whereas some reports discuss both in vitro and in vivo studies, the others report only the results of in vitro photothermal heating. Strikingly, NIR-II laser excitation of nanomaterials in the context of PTT has not been carried out. 3. Nanomaterials that allow host-guest complexation-based drug binding has not been applied for photochemotherapy therapy (PCTT).

The proposed project emerges from the lacunae observed in the (i) utilization of nanomaterials strongly absorbing near 1064 nm, which will possibly enable non-invasive treatment of breast cancer and (ii) photothermal heating-based controlled release of anticancer drugs from the smart nanocarrier, enabling bimodal treatment of cancer. Combining these strategies in applying one nanomaterial will enable a robust approach to chemophotothermal therapy.

c. Aims & Objective (in Bullets):

- To synthesize a new and novel class of Pr^{3+} based ferrites as NIR-II absorbing photothermal nanomaterials suitable for ablation of breast cancer cells by a low-power 1064 nm laser.
- To synthesize novel β -cyclodextrin derivatives suitable for coating on the NPs and enable host: guest association of capecitabine and 5-Fluorouracil their sustained release;
- To examine the in vitro anticancer activity of the drug-loaded nanocarriers on breast cancer cell lines and in vivo anti-breast cancer properties on mice; and
- To develop the drug-loaded NPs as PCTT agents.

d. Duration (MM/YYYY): 6 Months

e. Project Summary (1000 words):

(Separate page may be attached to justify the requirements)

The Expected Outcome of the Proposed Study

- The proposed study is centered on developing Praseodymium-based nanomaterials that will aid photothermal ablation of breast cancer cells. In addition, it will enable dose-controlled delivery of anticancer drugs viz., capecitabine, and 5-Fluorouracil that form host: guest complexes with β -cyclodextrin-modified polymer.
- A smart strategy to do a chemophotothermal cure of breast cancer.
- The process will be patented and a lead PCTT will be brought out. It will be in a state of readiness for translation into clinical trials in the future.

The Preliminary Work done so far

Our research group has synthesized a few Pr^{3+} nanoparticles with defined morphology, photoluminescence property, and absorption spectral band around 1000-1100 nm. The shape is a factor in governing the endocytosis of nanomaterials. Therefore, the shape-tuning of nanomaterials is a compelling necessity which is not easy in the case of all nanomaterials. We have worked on lanthanide-containing compounds to be formed in suitable sizes and shapes. Nevertheless, sulfide NPs of the lanthanides have not been attempted.

Scope of the Application indicating anticipated project and processes

Low power and non-invasive photothermal heating will be enabled. The surface modification of the NPS with the smart polymer allows an enhanced drug loading and release based on host: guest association and sustained delivery is a valuable addition to the **lanthanide** nanocarriers. The drug delivery agent is an expected highly biocompatible material and will open a new avenue in both PTT and drugs effectively targeting breast cancer. A new combined treatment procedure for the cure of breast cancer will be demonstrated at the animal level (in vivo).

f. Technical Details

- a. TRL : **NA**
- b. Methodology : **NA**
- c. Design & development : **NA**
- d. Facilities and Instrumentation required
 1. TEM(Transmission Electron Microscope)
 2. XPS(X-Ray Photoelectron Spectroscopy)
 3. TGA (Thermogravimetric Analysis)
 4. XRD(X-Ray Diffraction Analysis)
 5. MALDI (Matrix Assisted Laser Desorption/Ionization)
 6. 2D NMR
 7. ROESY
 8. In Vitro study MTT
 9. Flow Cytometry
- e. Consumables (Scientific materials) : **NA**

g. Expected output and outcome

- h. **Industry/Institute Collaboration** **If, yes**
 - (i) Name of the Collaborating Industry/Institute
 - (ii) Collaboration Details
 - (iii) Additional Details if any
- i. **Funding required from I-STEM (with justification):**

Details of Requirements & Mode of the Engagement: (Attach the quotation for the consumables)

(i) Short term Engagement:

a. Usage of testing/characterization facilities across the country (Characterization Mode)

i. Testing Charges

S.No	Instrumentation required	Charge per sample (Rs)	Total Cost(Rs)
1.	TEM(Transmission Electron Microscope)	2301	16107
2.	XPS(X-Ray Photoelectron Spectroscopy)	1770	12390
3.	TGA (Thermogravimetric Analysis)	1770	12390
4.	XRD(X-Ray Diffraction Analysis)	590	4130
5.	MALDI (Matrix Assisted Laser Desorption/Ionization)	708	1416
6.	2D NMR	1200	2400

7.	ROESY	1200	2400
8.	In Vitro study MTT	3000	42000
9.	Flow Cytometry	15000	105000
10.	In Vivo studies		100000
	TOTAL:		295833

- ii. Consumable charges
 - iii. Travel Cost (Boarding and Lodging, if any)
- b. Usage of fabrication and testing facilities across the country (Fabrication Mode) : **NA**
 - i. Fabrication and testing Charges
 - ii. Consumable charges (if any)
 - iii. Travel Cost (Boarding and Lodging, if any)
- (ii) Medium term Engagement: **NA**
 - a. Execution of project in any one of the Host Institution (Project Mode)
 - a. Fabrication and or testing Charges
 - b. Consumable charges (if any)
 - c. Travel Cost (Boarding and Lodging, if any)
 - b. Execution of project in Multi Host Institutions (Project Mode)
 - a. Fabrication and or testing Charges
 - b. Consumable charges (if any)
 - c. Travel Cost (Boarding and Lodging, if any)

(Round-trip to the Host Institution by 2nd class (Non-AC) railway via the nearest route)

Details of User's Bank Account:

(Please send a copy of the cancelled cheque/copy of the passbook carrying all the information needed)

Beneficiary Name (User's name): Muthuvijayan Enoch I V

PAN: AXQPM1504Q

Bank Account No. 917010078116269

Name of the Branch: Axis Bank
Irutupallam, Coimbatore, Tamilnadu

IFSC Code: UTIB0003730

Note: Proposed proposal must be executed within stipulated duration (max. 6 month) to avoid fund availability issues. Travel form will be provided by the I-STEM office. The users will submit the technical report, original invoice (duly signed by the Head of the Institution) raised by the Host Institution through I-STEM portal only along with a copy of the travel forms and original tickets through post to the Nodal Officer, I-STEM, Indian Institute of Science, Bangalore. A scan copy of all the documents may be sent in advance.