

CSR Proposal of Social Relevance**1. Title of the project:**

Development of biodegradable nanosystems for head and neck cancer theranostics

2. Background/Motivation:

Head and Neck cancer (HNC) remains the second most common forms of cancer affecting the middle aged and older population in India. Of all the etiological factors, smoking and chewing of tobacco contributes to about 70% of the HNCs. As per WHO, over 34.6% of the Indian adult population, predominantly men, consume tobacco in either smoke or smokeless form. Radiation, surgery and chemotherapy remain the golden standard treatment options for these cancers. Though efficient in handling the disease heterogeneity, high cost and adverse side effects render them insufficient. Most of cases in India are presented at the advanced stage, which has only about 40-50% chance of survival. Poverty, illiteracy, lack of access etc. pose critical challenges in management of these cancers. As per the cancer atlas project, Indian Council for Medical Research (ICMR), it is reported that 90% of HNCs cases in rural area belong to the lower/middle socio-economic class. Hence, there is a critical need for an affordable alternative therapeutic modality to treat HNCs. Nanotechnology has rapidly emerged as a potential interdisciplinary field extensively applied in cancer diagnosis and therapy. Nanoparticles also offer an additional advantage of preferential accumulation in tumor cells compared to the healthy cells via the enhanced permeation and retention effect due to the poor lymphatics and vasculature in cancer cells. The application of laser-driven Photothermal/Photodynamic therapy using plasmonic nanoparticles entrapping anti-cancer moieties has emerged as a cost-effective alternative for treating various cancer types. Photothermal therapy (PTT) converts the incident NIR light to heat with the help of photosensitive or plasmon resonant nanomaterials (like gold), resulting in localized heat generation and subsequent thermal ablation of cells. Photodynamic therapy (PDT) relies on ROS generation using photosensitizer dyes (such as IR-808, IR-780) upon NIR irradiation leading to apoptotic/necrotic cell death. A synergistic effect is exhibited when multiple treatment modalities are integrated in a single nano-platform. In this proposal, we intend to develop a nanopatform which can be used for integrating multimodal treatment exhibiting high targeting efficacy to the tumor microenvironment. For this, a Near infrared light (NIR) sensitive gold coated lipo-polymeric nanosystem will be developed, which can be incorporated with NIR dye / chemotherapeutic drug for a synergistic effect.

3. Objectives of the project:

The project aims to develop affordable nanotechnology based therapeutic modality for HNC theranostics. The objectives of the project are:

1. Development and characterization of NIR responsive gold coated lipo-polymeric nanosystems
2. Incorporation of NIR dye/ chemotherapeutic moieties within the gold coated lipo-polymeric nanosystems
3. *In vitro* evaluation of photothermal transduction efficacy, biocompatibility, photothermal mediated cytotoxicity and synergistic effect of combined therapy in cell lines
4. *In vivo* biodistribution, toxicity and anti-tumor efficacy of the developed nanosystems in mice tumor model

4. Brief methodology:

(A) Synthesis and characterization of nanoformulation for its physical properties such as shape, size, zeta potential and photothermal transduction efficiency using various characterization techniques like Dynamic Light Scattering (DLS), Scanning electron microscopy, Transmission electron microscopy,

(B) In vitro experiments:

1. Biocompatibility of these NPs will be performed at on various available normal cell lines with varying concentrations of NPs and optimal concentration range will be chosen for further laser mediated photo thermal therapy analysis.
2. Cellular uptake of these NPs in head and neck cancer cell lines
3. Photothermal mediated cytotoxic effect of these NPs in cancer cell lines (MTT assay, Live-dead assay, apoptosis and necrotic damages).

(C) In vivo experiments:

1. evaluation of biodistribution and tumoral uptake of NPs in mice tumor models
2. Investigation of the effect of nanoformulations with PTT/PDT over tumor induced mice model
3. Histology analysis of tumor regression
4. Evaluation of toxic and adverse effects in other organs using biochemical markers

5. Target population/Beneficiaries

The target population is both men and women of middle to older age in both urban and rural areas. The study yields a stable biocompatible nanosystem creating a scope for the direct clinical trials. The protocols for the development of the nanosystems will be optimised so that it is reproducible and scalable as per the requirements. The study involves addressing the theranostic efficacy of a multifunctional nanosystem for the treatment of the second most common forms of cancer in India, HNCs. Upon successful execution of the study, the results will enable development of novel therapies and techniques for the management of the disease.

6. Expected outcomes/ deliverables

1. This strategy may lead to the new affordable theranostic modality for the treatment of HNCs.
2. Liposome gold nanoparticles (Lipos-Au NPs) with a combination of Chemo-PTT/PDT may show additional synergistic effects and can improve therapeutic efficacy.
3. The particle-induced radiation by drug/dye incorporated NIR responsive NPs may be very effective to overcome the drug resistance as well as regrowth and metastasis of the cancer cells.
4. This approach will be valuable for developing a nontoxic and cost-effective treatment for chemoresistance and radio-resistant tumors in patients.

7. Timeline and budget:

	Year 1	Year 2	Year3	
Milestones	Synthesis and physico-chemical characterization of the nanosystem;	<i>In vitro</i> evaluation of anti-cancer efficacy in HNC cell lines	<i>In vivo</i> studies in mice tumor model	
Budget (in Rs lakhs)	9,26,400	9,86,400	9,86,400	
Proposed expenditure on	Year 1	Year 2	Year 3	Line total
a) Manpower	3,72,000	3,72,000	3,72,000	11,16,000
b) Contingency	2,00,000	2,00,000	2,00,000	6,00,000
c) Travel	1,00,000	1,00,000	1,00,000	3,00,000
d) Workshop/conference (Specific to project)	1,00,000	1,50,000	1,50,000	4,00,000
e) Equipment	0	0	0	0
f) Total	7,72,000	8,22,000	8,22,000	24,16,000
g) Overhead (20%)	1,54,400	1,64,400	1,64,400	4,83,200
Grand Total (f+g)	9,26,400	9,86,400	9,86,400	28,99,200

8. Proposer name and Designation

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