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27th August 2024

d. Details of research work duly signed by the applicant, for which the Sun Pharma award is cliaimed:

Cancer remains one of the leading causes of mortality worldwide, and a definitive cure is yet to be discovered. The primary objective of our laboratory is to identify and exploit strategic weaknesses in cancer signaling networks to uncover novel therapeutic targets. Our research spans a wide range of topics within cancer biology, both basic and applied, with a particular focus on cancer therapeutics, drug delivery, therapeutic resistance, and diagnostics.

Our team (Cancer Biology Lab) is a diverse group of researchers with expertise in cell and molecular biology, microbiology, bioinformatics, pharmacy, biochemistry, biotechnology, and chemoinformatics. We are constantly exploring new chemotherapeutic agents from both natural and synthetic sources and have recently expanded our work to include promising adjuvant therapies such as cancer immunotherapy and photothermal therapy. We are also developing advanced drug delivery systems, including liposomes, exosomes, and a variety of nanoparticles. By redesigning these nanocarriers for targeted therapy, we are evaluating various biomarkers to enhance the efficacy of these approaches.

Therapeutic resistance remains a major challenge in cancer treatment. Our research is focused on deciphering the molecular mechanisms that drive radio- and chemoresistance. We are investigating cancer stem cells, autophagy, and epigenetic factors to disrupt the regulatory mechanisms that promote resistance. In collaboration with oncologists, physicists, and engineers, we are also studying the molecular, biophysical, and bioelectrical changes that occur as cancer progresses from benign to malignant forms and as it acquires chemoresistance.

We made significant strides in cloning and characterizing genes involved in cancer progression, which not only serve as reliable diagnostic and prognostic markers but also open new avenues for gene-based cancer therapies. One notable discovery from his lab is the identification of MTA1s, which localizes in the cytoplasm, sequesters the estrogen receptor (ER), and enhances non-genomic responses of ER—a work published in Nature. Another important contribution is the discovery of a link between telomerase activity and cancer progression.

In recent years, our research has expanded to study natural compounds with anticancer potential. For example, we investigated the antineoplastic activity of thymoquinone and diosgenin, active ingredients from black cumin and fenugreek, against squamous cell carcinoma, breast, and colon cancer, both in vitro and in vivo. We also demonstrated that incorporating an anti-EGFR plus VEGFR strategy with chemotherapy is more effective in treating advanced breast cancer than either approach alone. Our research on Diacerein, an IL-6 inhibitor, showed that it offers a novel blueprint for cancer therapy by disrupting the IL-6/STAT3/MAPK/Akt network without toxic effects.

Recently, our Cancer Biology Lab has made significant advancements in nanoparticle-mediated drug delivery. For example, we have shown that celecoxib-loaded hydroxyapatite-chitosan

nanoparticles serve as a promising, effective, and safe means of delivering the drug in colon cancer therapy. We have also developed acidic milieu-sensitive multilamellar gold niosomes (Nio-Au) for the targeted delivery of Akt-siRNA and thymoquinone (TQ) in tamoxifen-resistant and Akt-overexpressing breast cancer cells. This innovative strategy, which combines siRNA and therapeutic drug delivery, shows significant potential for treating therapy-resistant cancers.

Additionally, our research has explored the role of multinucleated cells (MNCs) in chemoresistance. We have shown that MNCs, which express cancer stem cell markers, produce factors like VEGF and MIF that induce chemoresistance in drug-sensitive cells. This discovery presents new therapeutic opportunities.

My Lab's work on glioblastoma multiforme (GBM) has yielded groundbreaking results. My team identified Lumefantrine, an antimalarial drug, as a potential Fli-1 inhibitor that can reverse radio/temozolomide resistance in GBM. This discovery, supported by in vitro and in vivo studies, positions Lumefantrine as a promising therapeutic option for GBM.

Moreover, our recent studies, including "*Riboflavin-Induced DNA Damage and Anticancer Activity in Breast Cancer Cells under Visible Light: A TD-DFT and In Vitro Study*" (**Journal of Chemical Information and Modeling, 2024**), demonstrate the potential of riboflavin, activated by visible light, to selectively induce DNA damage in cancer cells while sparing normal cells. This innovative approach to photodynamic therapy offers a promising avenue for treating breast cancer. Additionally, his research on "*A Virtual Drug Discovery Screening Illuminates Campesterol as a Potent Estrogen Receptor Alpha Inhibitor in Breast Cancer*" (**Journal of Medicinal Chemistry, 2024**) showcases the effectiveness of integrating computational and experimental methodologies to discover new drug candidates. The identification of Campesterol as a potent antagonist of estrogen receptor alpha (ERα) presents a novel strategy for combating ERα-positive breast cancer.

In recognition of my contributions, as reflected in my publications in high-impact, Scopus-indexed journals, I believe that I am a deserving candidate for the Sun Pharma Award.

(Prof. Mahitosh Mandal)

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