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CRITICAL ASSESSMENT OF TOXICITY PROFILING, CELLULAR INTERNALIZATION AND BIOACCUMULATION OF ENGINEERED GRAPHENE BASED NANOCOMPOSITE IN VITRO FOR ADVANCEMENT IN BIOMEDICAL RESEARCH.

Although there is remarkable research efforts have been devoted in terms of fabricating and formulating graphene compound for a broad range of applications in healthcare and medical research such as drug delivery, cancer therapies and biosensing with ultimate goal of using it in clinical applications, however, the major bottleneck surrounding the applications of graphene is about their potential hazards and healthcare risk. Several studies have demonstrated cytotoxicity of various types of graphene/graphene derivatives in cell culture studies. Cytotoxicity refers to the ability of being toxic to living cells, and cells react to a cytotoxic compound in numerous ways. Previous work critically reviewed in vitro toxicity test procedures governing the underlying mechanisms of the cytotoxic effects induced by the nanomaterials, precisely linking the cytotoxic response to nanomaterials' structure, physicochemical properties, and their specific interactions within cell membrane and subcellular organelles. However, the correlation of the gathered results with the potential for negative effects of graphene/graphene derivatives on cells in vitro and in vivo remains uncertain. Many crucial questions must be answered before the graphene researchers' progress into the clinical research. We are aiming to provide an overview related to nanotoxicity, cellular uptake pathways, internalization and bioaccumulation evaluation of graphene based nanocomposites in vitro and discuss their findings with intention to disseminate the awareness of recent developments of biological application of graphene derivatives, their potential cytotoxicity, and methods in minimizing graphene based nanomaterials toxicity.

NANOMATERIALS-MEDIATED SIRNA DELIVERY SYSTEM FOR GENE THERAPY IN LUNG CANCER CELL

Gene therapy brings the new frontier in cancer treatment where new nanotechnology-based, safe and efficient delivery methods are also being developed. Double stranded RNA-mediated interference (RNAi) is a promising candidate in targeted cancer therapy in order to combat the limitations in conventional drug delivery system and adverse side effects of the chemotherapy regime. Small interfering RNA (siRNA) functions as potent therapeutic agent to induce gene silencing mechanism in RNA interference (RNAi). However, due to the limited delivery of siRNA through cell membrane, various nano-delivery systems have been developed to facilitate siRNA access to cytoplasm of the targeted cells. siRNA will be conjugated with nanomaterials that consist of superparamagnetic iron oxide nanoparticles (SPION) and quantum dots (QD) to enhance intracellular delivery across biological barriers and cellular uptake of the targeted cells. The characterizations of synthesized nanoparticles will be tested with X-Ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), Transmission Electron Microscopy (TEM), Dynamic Light Spectroscopy (DLS) and Vibrating Sample Magnetometer (VSM). The aim is that magnetic nanoparticles (SPIO) possessed the ability to package siRNA into nanoparticles for it to enter the

cancerous cell membrane easily. Semiconductor quantum dots (QDs) functions as multi-colour biological probes which helps in monitoring siRNA delivery. The fluorescent nanoparticles QD able to track delivery of nucleic acid, sort cell by degree of transfection and purify homogenously silenced subpopulations. Future study will observe cellular internalization of nanoparticles and gene silencing activity using Ultraviolet Visible Spectroscopy (UV-VIS), Confocal Laser Microscopy (CLFM), Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and flow cytometry. The formulation will be tested on two different cell lines, namely A549 human lung carcinoma and MRC5 human lung fibroblast cell. The toxicity test of the nanomaterials-siRNA formulations will be conducted using MTT assay. The incorporation of SPIO nanoparticles and QD in the siRNA delivery will help to provide efficient, multifunctional and nontoxic siRNA delivery agents for cancer.

GREEN SYNTHESIS ZNONPS FOR WATER TREATMENT: SYNTHESIS, CHARACTERIZATION, AND ANTIMICROBIAL ACTIVITIES

In wastewater treatment, chemical disinfection such as chlorination can react with various components in natural water leading to the byproduct formation that potentially hazardous to the environment which could be adversely affect human health. Metal oxide nanoparticles can be one of the alternatives to improve the wastewater treatment since it is not a strong oxidant and partly neutral to water. To minimize the use of chemicals and byproduct formation in wastewater treatment, we proposed the use of biological extract in the synthesis of nanoparticles via a green synthesis method, cost effective, renewable and eco-friendly approach. Therefore, this project aims to synthesis and study the structural and antibacterial properties of low cost and bio-based ZnONPs. In terms of application, the prepared biogenic ZnONPs will be tested for photocatalyst that suitable for water treatment to degrade the dyes and shows attractive antimicrobial properties over bacteria contaminants in wastewater.

DEVELOPMENT, CHARACTERIZATION AND BIOCOMPATIBILITY OF NANOMATERIAL BASED SCAFFOLDS FOR NEURAL TISSUE ENGINEERING

Neurodegenerative diseases are associated with progressive loss of neural and glial cells in the brain, leading to dysfunctions of the nervous system. Neural stem cells (NSCs) transplantation offers a great promise for treating these ailments, however, to date, there are still several issues needed to be solved prior to the use of NSCs into the clinical setting. One of the issues is the inability of the 2D culture system to fully mimic in vivo condition. Thus, the implementation of a 3D culture system that recapitulates neural development is necessary. Even though the 3D culture system is available, but the scaffolding materials for the cell growth is incapable to fulfil the specific requirement for stem cell therapy. Adding to this, most publications have used immortalized cell lines and also using unspecific scaffold material for the neural tissue. Carbon based scaffolds (CNTs/Graphene) have advantages to be developed as a scaffold for neural cells owing to the fact that they are electrically conductive. This allows for regulation of cell activity via electrical stimulations. Since cells are sensitive to the scaffold topographies,

tailoring scaffolds as 2D and 3D with isotropic and anisotropic structure, may help to direct NSCs to differentiate into the desired neural cell lineage. In this study, we aim to develop, characterize, optimize and assess biocompatibility of both 2D and 3D nanomaterial based scaffold for the growth and differentiation of NSCs. We choose to use primary NSCs from adult mouse to overcome the drawbacks of immortalized cell lines. Following culturing NSCs on the prepared scaffolds, we will assess the growth, proliferative capacity, morphological and functional changes in NSCs after induction of differentiation. Findings from this concerted effort of material science and basic neuroscience research will accelerate translational research in neuroregenerative medicine, neuropharmacology and neurotoxicology research.