CHEMICAL, BIOLOGICAL & MATERIALS ENGINEERING

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The University of Oklahoma
Norman, Oklahoma
2011 - 2012 Seminar Series

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ASSISTANT PROFESSOR OF CHEMICAL ENGINEERING GRADUATE FACULTY, HARRINGTON BIOMEDICAL ENGINEERING AND BIOLOGICAL DESIGN PROGRAM ARIZONA STATE UNIVERSITY TEMPE, ARIZONA

Will present a seminar on

"SYNERGISTIC APPROACHES IN MOLECULAR AND NANOSCALE THERAPEUTICS AND DELIVERY SYSTEMS FOR CANCER DISEASES?"

Cancer diseases place an enormous burden on the human condition. While surgery and radiation therapy are common primary interventions for localized disease, new developments in chemotherapy, gene therapy, immunotherapy, are under investigation in cases of recurrent, aggressive and metastatic disease. The complexity and heterogeneity associated with advanced cancer diseases manifest as multiple resistance mechanisms to treatment. This, in turn, necessitates approaches that act synergistically in order to overcome these resistances, leading to effective cancer cell death.

Research in my laboratory involves the discovery and delivery of synergistic treatments for enhancing the efficacy of molecular and nanoscale therapeutics in three related areas: (1) polymer-mediated gene delivery, (2) nanoparticle-induced hyperthermia, and (3) discovery and nanoparticle-mediated delivery chemotherapeutic drug combinations, all focused on enhancing apoptosis (programmed suicide) of cancer cells.

Gene therapy involves the administration of genetic material in order to overcome the consequences due to genetic mutations that characterize several diseases, including cancer. Polymers are safer alternatives to viral delivery vectors, but polymer-mediated delivery typically suffers from low efficacies of protein expression. The bulk of this presentation will describe the synergistic use of materials discovery together with anti-cancer chemotherapeutic drugs for enhancing the efficacy of polymer-mediated gene delivery. We first employed combinatorial syntheses and parallel screening in order to rapidly synthesize and identify polymers that demonstrated higher transgene (e.g. GFP or luciferase) expression and lower cytotoxicities compared to current polymeric standards. At the sub-cellular level, escape from intracellular vesicles (endolysozomal compartments), transport in the cytoplasm, and nuclear entry are barriers that significantly limit the efficacy of polymeric delivery systems. Chemotherapeutic mediators that modulate intracellular trafficking, nuclear import, and cell cycle dynamics were therefore employed for overcoming these barriers leading to enhanced polymermediated transgene expression. This strategy, in which anti-cancer chemotherapeutic modulators were employed to increase the expression of the pro-apoptotic p53 protein, was employed to enhance cancer cell death. As an orthogonal example of synergistic approaches, polymers developed in our laboratory were employed for enhancing adenovirus-mediated gene expression, and therefore death, in bladder cancer cells that resist viral infection.

I will also briefly introduce our research on gold nanorod-polypeptide based plasmonic 'nanomatrices' which are capable of simultaneously administering hyperthermia and chemotherapeutic drugs for ablation of cancer cells. Finally, I will introduce our work on the discovery and nanoparticle-mediated delivery of clinically relevant chemotherapeutic sensitizers of TRAIL-induced apoptosis in prostate and pancreatic cancer cells. The use of microfluidic devices in facilitating this drug discovery process will also be briefly mentioned.

Our research demonstrates that a synergistic approach which combines molecular engineering and cancer cell biology can be employed for the discovery, optimization, and delivery of combination treatments leading to enhanced efficacies of molecular and nanoscale systems. Ongoing and future work involves detailed mechanistic elucidation of these findings and their evaluation using appropriate models in vivo. Materials and mechanisms from our research also have the potential to impact other disciplines in medicine and biotechnology.

THURSDAY, APRIL 5, 2012 COOKIES AND COFFEE -- 2:45 P.M. SEMINAR -- 3:00 P.M. SARKEYS ENERGY CENTER, ROOM M-204

THIS IS A REQUIRED SEMINAR FOR CHE 5971

Accommodations on the basis of disability are available by contacting the office before the event.