

Synopsis Seminar

Seminar Title	: Combinatorial approaches of computational genomics and nanoengineered hydrocolloid based multi modal therapeutic intervention for NSCLC
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Venue	: LS Meeting Room
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Abstract	<p>: In the current study, we used a meta-analysis of transcriptome data to comprehensively identify 678 overlapping genes that were expressed differently in NSCLC compared to normal lung tissues. Enrichment analysis was implemented to identify the signaling pathways and pertinent activities of differentially expressed genes (DEGs). We subsequently identified the greatest clique centrality (MCC) approach to screen CENPF, TOP2A, NUF2, PTTG1, CCNB1, CEP55, CDC20, PERP, and DSG2 as hub genes. Furthermore, sorafenib (SF) was predicted by a drug-gene interaction network to be a viable therapeutic candidate to counteract the dysregulated effects of oncogenes. According to molecular docking studies, SF has a higher binding affinity for DSG2 [$\Delta G = -7.1$ kcal/mol], PERP [$\Delta G = -8.6$ kcal/mol], and CCNB1 [$\Delta G = -8.0$ kcal/mol]. We further encapsulated SF within the hollow matrix of HMSNs by a novel, quick and economical procedure to optimize their synthesis by using the RSM-CCD approach. The drug loading efficiency of SF-MSNs and SF-HMSNs was 13.71 ± 0.33 % and 51.31 ± 0.94 % respectively. In-vitro cell culture studies were done to explore the anti-tumorigenic prospects of free and encapsulated SF. Cell cytotoxicity was assessed by MTT assay against A549 cells, indicating enhanced toxicity for optimized SF-HMSNs. IC50 value substantially decreased from 10.5 to 5.8 μg/ml (1.8 fold decrease) after encapsulation. In this study, chlorophyll was naturally extracted from the leaves of <i>Murraya koenigii</i> and the extraction process was optimized using GRA-APSO design. It was encapsulated within pluronic 127, a commercial surfactant that increases hydrophilicity. This formulation displayed excellent biocompatibility and possibility in the field of cancer imaging. Additionally, without impairing the biological system, the water-soluble fluorescent pearls attained a three-fledged action of multi-color imaging, in vitro cell photostability, and migration, acting as a biocompatible system in cancer biology. Histological and biochemical studies showed that pluronic coated chlorophyll were not overtly harmful to mice, even when given at multiple doses. The development of nanofibrous PEC of CS and pectin at varying volume ratios was successfully accomplished using entropy-driven self-assembly. Additionally, a nanofibrous polyelectrolyte (PEC) complex comprising pectin (Pec) and chitosan (CS) was made at various volumetric ratios. In order to improve the mechanical characteristics of hydrogels and achieve long-term therapeutic efficacy and sustained drug release, nanofibers were added to CS-based injectable thermoresponsive hydrogel. The desired amount of OE-P127 and SF was then added to the thermogel matrix to enable the diagnosis and treatment of NSCLC at the same time. Hydrogel samples with CS and pectin (1:3) showed superior injectability, degradability, controlled release kinetics, higher viscosity, and faster gelation. The uniform dispersion of chlorophyll within the hydrogel matrix was validated by the red FL of S8 hydrogel at 588 nm. Blood compatibility tests showed that the as-synthesised thermogels had a good hemocompatible profile. The hydrogel versions made with CS: Pec (1: 3) outperformed their CS: Pec (1: 5) counterparts in terms of swelling ratio (19.59), degradability, and sustained SF release (40%). According to the MTT assay and live/dead labeling, the SF-loaded hydrogel variant significantly cytotoxicity affected A549 cells due to its gradual and prolonged release of SF. The produced hydrogel structures (S5–S8) and their predecessors were found to be cytocompatible by the MTT assay and live/dead staining, and the anti-proliferative effects of S5–S7 hydrogel on A549 cells were exclusively ascribed to the released SF. The FL of chlorophyll formulation was utilized in conjunction with CLSM to track the cellular uptake of SF. Furthermore, by effectively differentiating between live and apoptotic cells under CLSM, the FL labeling property of chlorophyll outperformed the application of traditional dyes. The expression levels of the oncogenes CCNB1, CENPF, DSG2 and PERP in A549 cells were significantly reduced by both free SF and the S8 hydrogel. In conclusion, the combination of therapeutic and diagnostic components in one system opens up new possibilities of injectable thermogels for use in cancer theranostics.</p>

Key Words: Non-small cell lung cancer, HMSN nanoparticle, SF, Chlorophyll, biomarkers, targeted drug delivery, bioimaging, injectable thermogels, theranostics