Docetaxel-Loaded Liquid Crystalline Nanoparticles Wrapped with Graphene Oxide for Effective Chemo-Photothermal Therapy of Metastatic Prostate Cancer Cells
R. K. Thapa¹, H. T. Nguyen¹, H. B. Ruttala¹, T. Ramasamy¹, D. S. Kim², H. G. Choi², C. S. Yong¹, J. O. Kim¹
¹Yeungnam University, ²Hanyang University

Purpose
Prostate cancer is one of the most common malignancy affecting men worldwide. Docetaxel (DTX) is recommended by the US Food and Drug Administration (FDA) as a first line treatment option for castration-resistant prostate cancer. However, conventional formulation has minor benefits and potentially causes multiple adverse drug reactions with high risk of resistance development. Monoolein-based liquid crystalline nanoparticles (LCN) and graphene oxide (GO) are emerging drug delivery carriers that could respectively load hydrophobic drug and produce near-infrared induced photothermal effects beneficial for cancer treatment. Hence, we report preparation of PEGylated LCN loaded with DTX and wrapped with GO, PEG-GO/LCN/DTX, for effective chemo-photothermal therapy of metastatic prostate cancer cells.

Methods
GO was prepared using modified Hummer’s method. GO/LCN/DTX was prepared by melting the hydrophobic phase (monoolein, poloxamer 407 and DTX) followed by addition of hydrophilic phase (GO dispersion); vortexing and probe sonication for appropriate time. Chitosan-PEG was added to the dispersion, followed by sonication to prepared PEG-GO/LCN/DTX. Characterization was performed by particle size and zeta potential analyses, transmission electron microscopy (TEM), entrapment efficiency (EE) and loading capacity (LC) analyses, and in vitro drug release profiles. In addition, in vitro cellular uptake, cytotoxicity, anti-migration and apoptosis induction effects were determined in prostate cancer cells.

Results
Prepared formulation exhibited small particle size (< 250 nm), high drug loading capacity (~ 15%), and efficient near infrared (NIR) light induced thermal heat. TEM images present preparation of appropriate drug loaded nanoparticles. pH dependent drug release profile for DTX was evident. Importantly, PEG-GO/LCN/DTX was successfully accumulated in prostate cancer cells, and exhibited potent apoptotic and anti-migration effects, mediated by the combination of the anticancer effect of DTX and thermal heat from NIR exposure of GO. Enhanced expression of pro-apoptotic markers (Bax, p53, p21) and reduction in anti-apoptotic marker (BCl2) upon treatment with PEG-GO/LCN/DTX+NIR suggest its high efficacy in prostate cancer treatment.

Conclusion
Prepared PEG-GO/LCN/DTX possessed appropriate particle size, drug loading capacity, and ability to induce photothermal effects. High cellular uptake and apoptosis in prostate cancer cells suggest it as an effective drug delivery system. Hence, PEG-GO/LCN/DTX is a potential system for effective treatment of metastatic prostate cancer.