

31st Nano Congress for Future Advancements

&

13th Edition of International Conference on Nanomedicine and Advanced Drug Delivery

August 29-30, 2019 London, UK

Modulation of tumor microenvironment by tumor vascular network reconstruction for improved anti-tumor effect

Jing Yao

Pharmaceutical University, China

Statement of the Problem: Tumor vascularity plays an important regulatory role in supporting the proliferation of tumor cells and constructing tumor microenvironment. The once-popular strategy of “starving tumors” by blocking neovascularization was proved to increase the risk of mutation and metastasis, which resulted from the aggravated hypoxia and insufficient drug delivery by the blocked vascular access. While the theory of vessel normalization required a timespan (window) characterized by the balance between pro- and anti- angiogenic factors, in which the structurally and functionally normalized vessels were expected to increase oxygen supply and drug delivery. However, the window is normally transient, difficult to monitor and utilize. The dilemma of the two established theory concerning vascular issues is urgently needed to be addressed.

Methodology & Theoretical Orientation: The anti-angiogenic polysaccharide LMWH was derived to be bioactive drug carriers for tumor nanotherapy. LMWH-Gemcitabine-Cholesterol nanodrug (LGC) integrated with paclitaxel was applied to precisely regulate tumor angiogenesis *via* metronomic chemotherapy. Moreover, pre-tailored LMWH-chrysin and mitochondrial damage KLA peptide were assembled by small-molecular doxorubicin, to be the supramolecular nanocomplex (LKD).

Findings: LGC nanodrugs could significantly prolong the window and enhance the extent of the vessel normalization, and meanwhile the synchronous administration of paclitaxel led to the significant tumor control. Dominated by doxorubicin, LKD nanocomplex yield favorable drug loading and blood stability, while smart disassembly in tumor milieu resulted in dual cells- (endothelial and tumor cells) /organelle (mitochondria and nucleus)-targeted antitumor efficacy. Through the recovery of tumor vessels, these nanodrugs reconstructed tumor microenvironment and thus yielded remarkable tumor growth suppression.

Conclusion & Significance: Owing to the intimate crosstalk between tumor cells and endothelial cells, LGC and LKD nanodrugs could improve the tumor microenvironment by accurately balancing the pro- and anti- vascular factors, which benefited for restoring oxygen supply, improving nanodrug distribution and curbing the tumor progression.