

22<sup>nd</sup> International Conference and Expo on**NANOSCIENCE AND MOLECULAR NANOTECHNOLOGY**

November 06-08, 2017 | Frankfurt, Germany

**Combinational strategy via co-delivery of drugs and siRNA by layered double hydroxide-based nanocomposites in cancer therapy**

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Chemotherapy is one of most common cancer treatments in clinics. In most cases, the clinical responses show that the efficacy of chemotherapy is limited by the development of multidrug resistance (MDR) in cancer cells during a long period of treatment. Target-specific delivery and sustained release of anticancer agents and siRNA has attracted considerable research interest in cancer chemotherapy. It is clear that the single treatment by either anticancer drug or siRNA delivered by nanocarriers can only achieve limited success in overcoming the MDR of cancer cells. Thus, the development of an effective strategy to overcome the multidrug resistance in chemotherapy remains a major challenge in the treatment of cancers, where co-delivery of anticancer drugs and siRNA would be a promising strategy. For this purpose, layered double hydroxides (LDHs), a family of anionic clay materials, have been examined as an example for simultaneous drug and gene delivery by using their unique properties. Our strategy is to combine two different types of anticancer therapeutics for effective cancer treatment. For example, 5-fluorouracil (5-FU) and siRNAs were co-loaded and then co-delivered to treat cancer cells, as illustrated in Scheme 1. Our data clearly indicate that LDH nanoparticles (NPs) can efficiently co-deliver 5-FU and siRNA into MCF-7 and U2OS cells and combination treatment with siRNA and 5-FU leads to significantly higher cytotoxicity to three cancer cell lines (MCF-7, U2OS and HCT-116), compared to the single treatment with either siRNA or 5-FU. Therefore, co-delivery of siRNAs and anticancer drugs by LDHs synergistically enhances the efficacy in these cancer treatments and has great potential as a novel approach for effective cancer treatment.

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