Development of nano-prodrug@hydrogel materials for locoregional therapy

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Malignant skin ulcerations are caused by skin cancer or metastatic spread to the skin, resulting in the loss of epithelial tissues. In the present study, we aimed to develop nano-prodrug@hydrogel materials for locoregional therapy of malignant skin ulcerations. Compared to drugs in the molecular state, nano-prodrugs (NPDs), which are composed of only prodrug molecules, have high pharmaceutical activity due to high permeability to the tissue. Polydopamine nanoparticles (PDA-NPs) are introduced into poly(N-isopropylacrylamide) (pNIPAM) hydrogel to fabricate a PDA-NPs/PNIPAM hydrogel system. PDA-NPs, as a near infrared (NIR) sensitive material, can be heated under 808 nm NIR light and shrink the temperature sensitive pNIPAM hydrogel. Thus, this system is designed that can use NIR light to rapidly excite and release NPDs on demand. Here, we reported the fabrication of PDA-NPs/pNIPAM hydrogel loaded with SN-38-cholesterol nano-prodrugs (SN-38-chol NPDs).

SN-38-chol NPDs were prepared by reprecipitation method[1].The size of the NPDs was about 120 nm (Fig. 1 (b)). PDA-NPs/pNIPAM hydrogel drug delivery system loaded with SN-38-chol NPDs was successfully fabricated (Fig. 1 (c)). The drug loading of the SN-38-chol NPDs@hydrogel was about 0.05 mg/g (drug weight/hydrogel weight), indicating a good drug loading capacity of the system. To evaluate *in vitro* cytostatic activity, SN-38-chol NPDs dispersion and SN-38-chol NPDs@hydrogel were applied to HCT-116 (human colon cancer) cell at the same final concentration and incubated for 48 h. As a result, SN-38-chol NPDs dispersion and the SN-38-chol NPDs@hydrogel showed similar cytostatic activity (Fig. 2).

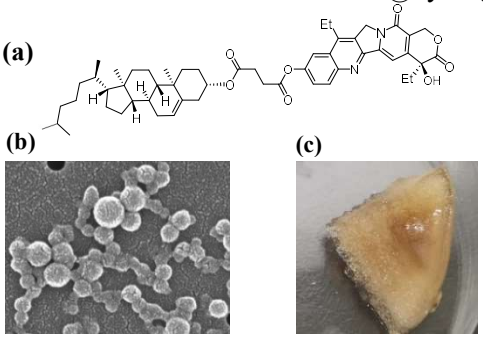

Fig.1 (a) Chemical structure of SN-38-chol (b) SEM image of SN-38-chol NPs (c) SN-38-chol NPs@hydrogel.

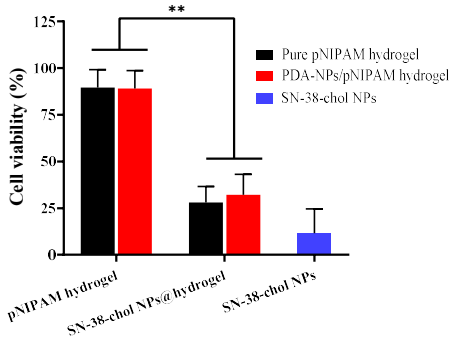

Fig.2 *In vitro* cytostatic activity at 48h.

Reference: 1) H. Kasai *et al.*, *Angew. Chem., Int. Ed.* 2012, **51**, 10315.