A versatile pH-responsive hyaluronic acid based multiple drug delivery system for cancer treatment

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Nanomedicine has recently experienced unprecedented growth and a wide range of engineered nanoplatforms are used for cancer drug transportation due to their small size, relatively big surface area and flexible surface functionalization.[1] Efficacy can be further improved by controlled release through stimulation by the tumour microenvironment.[2]

Here we have developed a hyaluronic acid (HA) nanoparticle (NPs) which can be conjugated with an acid-cleavable boronic acid functional group. HA also has high affinity for CD44+ overexpressed by cancer cells.[3] This strategy has been assessed for formulations with both bortezomib, used in treating multiple myeloma, and a doxorubicin prodrug, used for treatment across many cancer indications. The boronic easter is stable under physiological condition but is cleavable under acidic conditions in tumour [4].

Overall, this presentation will discuss the design and characteristics of pH-responsive HA nanocarriers and its anticancer application in two cancer models representing triple negative breast cancer and multiple myeloma. The transmission electron microscopy showed the spheric and well dispersed nanoparticles with size in 50-100 nm. Nuclear magnetic resonance spectroscopy (NMR) showed the HA and bortezomib/doxorubicin conjugates are pH cleavable release behaviour under acidic pH (5.5) but more stable under pH 7.4. The doxorubicin HA nanoparticles showed improved effects in 4T1 bearing breast cancer (Figure 1) with longer survival time. The tumour size was reduced along with metastasis reduction in lung and negligible body weight loss compared to the treatment with free doxorubicin. The Cy7 labelled HA NPs had good target and accumulation in C57BL.KaLwRijHsd multiple myeloma cancer model (Figure 2). The bortezomib loaded HA NPs will be used to treat the developed myeloma cancer model, and the outcome will be presented in the upcoming presentation.

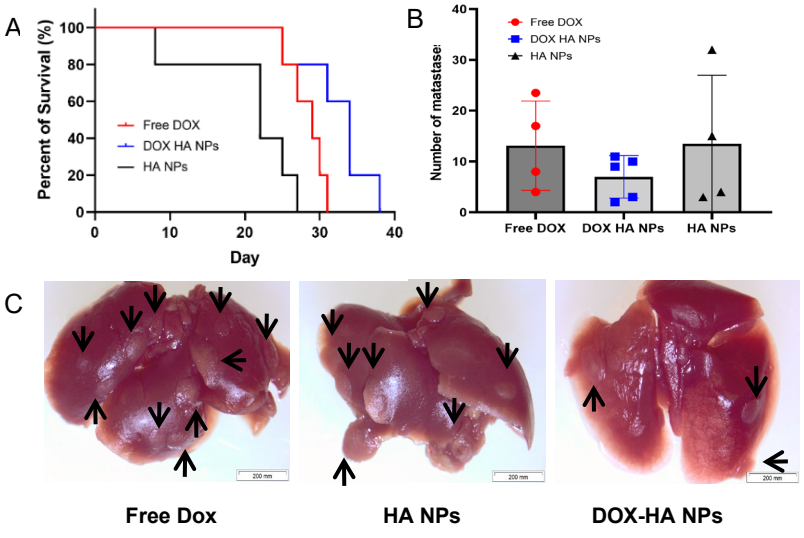

Figure 1 (A) The Survival rate of 4T1 tumour-bearing mice following intravenous injection of free DOX, HA NPs and DOX HA NPs; (B) Numbers of lung metastases per mouse for each group; (C) The lung metastatic images of in different treatments. (Arrows indicate lung metastases)

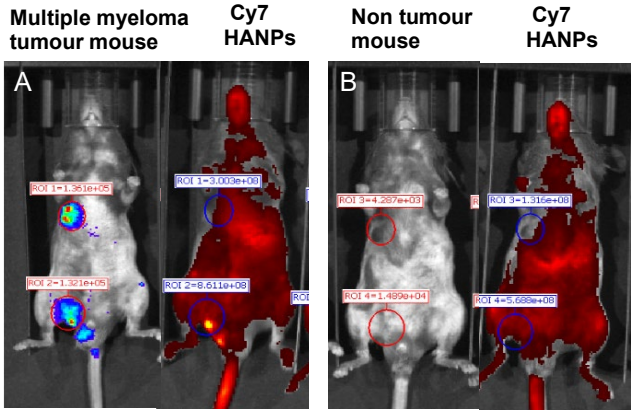

Figure 2 Representative biodistribution image of Cy7 HA nanoparticles accumulating in multiple myeloma tumour mouse (A) and healthy mouse (B). (Bioluminescence measured the tumour and fluorescence measured existence of Cy7 HA NPs)

Reference:
[1] Nature nanotechnology, vol. 14, no. 11, pp. 1007-1017, 2019.
[2] Nature nanotechnology, vol. 16, no. 1, pp. 104-113, 2021.
[3] Molecules, vol. 25, no. 18, p. 4323, 2020.
[4] Pharmaceutics, vol. 11, no. 7, p. 301, 2019.