Yuan-Chia Chang et al., J Nanomed Nanotechnol 2017, 8:4(Suppl)
DOI: 10.4172/2157-7439-C1-050

The cisplatin-HA nanocomplexes for novel lymphatic delivery system

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Head and neck carcinoma is the sixth most common cancer worldwide. 50-60% of patients with stage III or IV disease present locoregional recurrence within 2 years. Given the limitations of surgical resection and the low effectiveness of radiotherapy and chemotherapy, the treatment of lymphatic metastatic tumors remains a great challenge. Nanoparticles are potential tools for the lymphatic drug delivery but the major hurdle of existing nanoparticles is poorly retained in the draining lymph nodes following injection (less than 2% injected dose). Hyaluronic Acid (HA) is seen as an ideal carrier for the treatment of lymphatic tumors due to it is the ligand for CD44 receptor and cleared primarily by the lymphatic system. In this work, we performed an improved Cisplatin-incorporated HA nanocomplexes (CPHC008) and evaluated the potential use as carriers for lymphatic drug delivery and tumor lymphatic metastasis inhibition. HA/Boc-His/PEG graft copolymers were mixed with Cisplatin (CDDP) followed by stirring. The mixture was sonicated and purified by ultrafiltration and 0.22 μm filtration to form the CDDP incorporated HA nanocomplexes (CPHC008). The size and zeta potential were 200 nm and -30 mV respectively. Transmission electron microscopy showed the formation of spherical nanoparticles. The drug release behavior from CPHC008 in PBS showed more stable than native HANP. *In vitro* cellular binding/uptake confirmed the CPHC008 had specificity target the CD44 positive cells. As a result of active targeting properties, CPHC008 could increase platinum levels in the cervical lymph nodes and against lymph node metastases was significant. Taken together, we have designed a HA-based nanocomplexes to increase platinum levels in the lymphatics, where early metastasis is most likely to occur. This lymphatic delivery platform may offer significant advantages for the use of platinum medicines in the management of locally carcinoma, treating microscopic lymph node disease with better efficacy than current high-dose systemic chemotherapy.

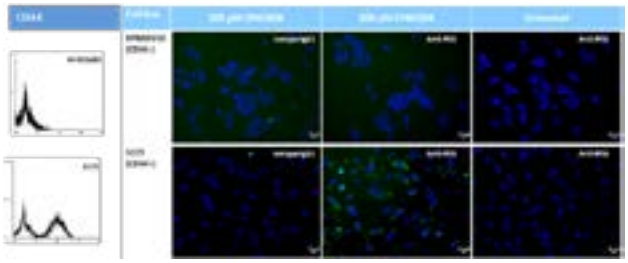

Figure: In vitro cellular binding/uptake assay confirmed the CPHC008 have specificity target the CD44 positive cells

Treatment	Metastatic rate (%) after treatment
Vehicle control	90%
CDDP (3 mg Pt/kg, iv)	75%
CPHC008 (3 mg Pt/kg, buccal injection)	10%

Table: Antitumor activity of CPHC008 against metastatic tumors in mice bearing SAS-LN

Biography

Yuan-Chia Chang is a senior researcher of Biomedical Technology and Device Research Laboratories (BDL), Industrial Technology Research Institute (ITRI), Tawan, R.O.C. ITRI is a nonprofit R&D organization engaging in applied research and technical services. The vision of BDL is to become a premier global hub for the research and development of innovation-based biomedical technology and medical devices. Dr. Chang graduated from Chang Gung University in Medical Technology, obtained his MS degree in Biomedical Engineering department from National Yang-Ming University, and obtained his PhD degree in Chemical Engineering from National Tsing-Hua University in Taiwan, R.O.C. He majors and specialties are focused on bio-polymer application and drug delivery system.

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