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HA-based nanocomplexes for head and neck cancer with lymphatic metastasis

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Statement of the Problem: Head and Neck Squamous Cell Cancer (HNSCC) is the sixth most common cancer in the world. Current therapeutic approaches in treating HNSCC patients are limited in choice and efficacy, hampered by physiological side effects, as well as risks of recurrence. Even with surgical resection, microscopic tumor may remain and lead to locoregional recurrence. Moreover, systemic chemotherapy cannot effectively reach the lymphatic system without showing dose-limiting toxicities. Therefore, treatment of lymphatic metastasis remains a great challenge.

Methodology & Theoretical Orientation: HA/Boc-His/PEG graft copolymers were mixed with cisplatin followed by stirring for 72 h. The mixture was sonicated and purified to form CPHC008. The size distribution and drug release from CPHC008 were evaluated by dynamic light scattering measurement and dialysis method. To evaluate the lymph node delivery, mice were injected intravenously with CPHC008 and cervical lymph nodes were collected to analyze the platinum content by ICP-MS. To investigate the inhibition of lymphatic metastasis, CPHC008 were injected intravenously into mice bearing SAS-LN tumor with cervical metastasis. The cervical nodes were collected to evaluate metastasis by bioluminescence image using IVIS.

Findings: The particles size and zeta potential of CPHC008 were 200 nm and -30 mV respectively. The drug release behavior from CPHC008 in PBS showed more stable than native HA-based nanoparticles. *In vitro* cellular binding/uptake demonstrated CPHC008 could target the CD44+ cells. As a result of CD44-targeting, CPHC008 could increase platinum levels in the cervical nodes and inhibit lymphatic metastases significantly.

Conclusion & Significance: We have designed a HA-based nanocomplex 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 advanced HNSCC, treating microscopic lymph node disease with better efficacy than current high-dose systemic chemotherapy.

Biography

Chih-Peng Liu is a Senior Researcher of Biomedical Technology and Device Research Laboratories (BDL), Industrial Technology Research Institute (ITRI). 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. He received his Bachelor of Pharmacy at Taipei Medical University and obtained his MS and PhD in Pharmacology from National Yang-Ming University. His majors and specialties are focused on pharmacokinetics (PK) and pharmacodynamics (PD) evaluation of drug development. Currently, he is a Deputy Project Manager of Drug Delivery Division and responsible for the novel hyaluronan-based nanocarriers development.

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