Anti-tumor and Anti-metastasis Activities of Dichloro (1, 2-diaminocyclohexane) Platinum (II) (DACHPt)-Incorporated Hyaluronic Acid Nanoparticles (DACHPt/HANPs) in Colon Cancer and Melanoma Model *in vivo*

Shih-Ta Chen, Tai-ju Hsieh, Chun-Min Liu, Ya-Chin Lo, Chih-Peng Liu, and Hsiang-Wen Tseng

Biomedical Technology and Device Research Laboratories, Industrial Technology Research Institute, Hsinchu, Taiwan, ROC

godzilla@itri.org.tw

Abstract

Nanotechnology provides many potential benefits to cross the hurdle of cancer therapy, such as delivering drugs to cancer cells, or reducing adverse side effects of toxicity. Nanoparticles can passively accumulate in the tumor through the leakage of endothelium by the enhanced permeability and retention (EPR) effect, or further actively target the specific cancer cells via various receptors expressing on the cell surface of cancers. Hyaluronic acids (HA) are high biocompatible macromolecules, suited to application in biomedicine, and as ligands binding to many receptors (CD44, ICAM etc.). Here, we investigated a novel type of HA polymer based delivery system, the dichloro (1, 2- diaminocyclohexane) platinum (II) (DACHPt)- incorporated HA comb-like polymer (DACHPt/HANPs) with anti-tumor and anti-metastasis effects in colon cancer and melanoma. We used HA-Boc-His polymer to play a role in the particle release and stabilization, providing the hydrophobicity as a driving force for the metal-polymer ionic complex formation between the platinum of DACHPt and the carboxyl group on the HA. In the present study, in vivo experiments of anti-tumor activity were performed on human colon cancer cell line, HT29 xenograft tumor model. Intravenously administered DACHPt/HANPs suppressed tumor growth significantly than free oxaliplatin, the standard chemotherapy of colon cancer. The tumor growth inhibition (TGI) of HT29 tumor treated by oxaliplatin or DACHPt/HANPs was 2±14 % or 60±8 %. DACHPt/HANPs not only demonstrated effective tumor growth inhibition of colon cancer, but also inhibited melanoma lymphatic metastasis. The volume of lymph nodes in mice subcutaneous injected of DACHPt/HANPs or intravenous injected of oxaliplatin were 34±20 or 73±46 mm^3 in the murine melanoma cell line, B16-F10-luc2 spontaneous lymphatic metastasis model. Our study showed that DACHPt/HANPs considerably increased the anti-tumor and anti-metastasis activities, and the HA based DACHPt ionic nanoparticles are promising for the drug delivery system.

References

[1] Cabral H, ACS Nano. 2015 May 26;9(5):4957-67

[2] Endo K, Cancer Sci. 2013 Mar;104(3):369-74.

Figures