Quantitative analysis of $Gd@C_{82}(OH)_{22}$ and cisplatin uptake in single cells by inductively coupled plasma mass spectrometry

Ling-Na Zheng, Meng Wang[1,*], Wei-Yue Feng
CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, CAS Key Laboratory of Nuclear Radiation andNuclear Energy Technology, Institute of High Energy Physics, Chinese Academy of Sciences, Beijing 100049, China
Email: wangmeng@ihep.ac.cn

ABSTRACT:

As one of themost fatal diseases around the world, cancer is usually treated with chemotherapy, radiation therapy, and surgery.Cisplatin is a common drug that has been widelyused in the treatment of many different solid tumors.Although cisplatin is an effective drug against solid tumor, clinic applications of cisplatin suffer from serious side-effects. Furthermore, the treatment always deteriorates due to tumor resistance to cisplatin. As a novel endohedralhydroxylatedmetallofullerenol nanoparticle, $Gd@C_{82}(OH)_{22}$ has demonstrated recently to be a promising antineoplastic agent [1]. It could inhibit tumor effectively with relatively low doses and has low toxicity to cells.

The quantitative measurement of the cellular uptake of drugs is of great importance for the elucidation of drug action, drug safety, and drug resistance. In mechanism investigation and clinical diagnostics, extremely sensitive analytical methods, down to single cells, may provide the most important information for personalized therapies. However, analysis of metal drugs in single cells is still a great challenge. Recently, as one of the most advanced and sensitive means for ultra-trace element analysis,inductively coupled plasma-mass spectrometry (ICP-MS) has been introduced and become a promising method for analysis of intracellular elements at single cell level[2-3].

In this study, we determined intracellular $Gd@C_{82}(OH)_{22}$ and cisplatin after treatment ofHela and 16HBE cells by single cell inductively coupled plasma-mass spectrometry (SC-ICP-MS), which could provide quantitative information at a single-cell level. The cell digestion method validated the accuracy of the SC-ICP-MS. The concentrations of $Gd@C_{82}(OH)_{22}$ andcisplatinin cells at different exposure time and doses were studied.Our data show that$Gd@C_{82}(OH)_{22}$ has higher bioavailability and lower toxicity than cisplatin*in vitro*, and thus make it possible to inhibit tumor at a low dose.The capability of ICP-MS for single cell analysis was thus demonstrated here.The SC-ICP-MS is promising complement to available methods for single cell analysis and is hopeful to be further applied to biomedical research [4].

KEYWORD: Cisplatin; $Gd@C_{82}(OH)_{22}$; Single cell; ICP-MS; Quantitative analysis

REFERENCE:

1. Chen, C.; Xing, G.; Wang, J.et al.. Nano Letter, 2005, 5 (10), 2050-2057.
2. Zheng, L.-N.; Wang, M.; Wang, B. et al.. Talanta, 2013, 116 (0), 782-787.
3. Wang, M.; Zheng, L.-N.; Wang, B. et al. Analytical Chemistry, 2014, 86 (20), 10252-10256.
4. Zheng, L.-N.; Wang, M.; Zhao, L.-C. et al. Analytical Bioanalytical Chemistry, 2015, 407 (9),2383-2391.

ACKNOWLEDGMENT: This work was supported by the National Basic ResearchProgram (973 program: 2011CB933403), and the National Natural Science Foundationof China (21175136, 11275214, 11375211, and 11475195).