ORIGINAL ARTICLE

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^{99m}Tc-sestamibi to monitor treatment with antisense oligodeoxynucleotide complementary to MRP mRNA in human breast cancer cells

Seigo KINUYA,* Jingming BAI,* Kazuhiro SHIBA,** Kunihiko YOKOYAMA,* Hirofumi MORI,**
Makoto FUKUOKA,* Naoto WATANABE,*** Noriyuki SHUKE,****
Takatoshi MICHIGISHI* and Norihisa TONAMI*

*Department of Biotracer Medicine, Kanazawa University Graduate School of Medical Sciences
**Radioisotope Center, Kanazawa University
***Department of Radiology, Toyama Medical and Pharmaceutical University
****Department of Radiology, Asahikawa Medical College

Objective: Technetium-99m sestamibi (MIBI) has been utilized to evaluate multi-drug resistance (MDR) phenomenon of malignant tumors and to predict chemotherapeutic effects on them. The current investigation examined the possibility of monitoring changes with respect to mRNA expression of multi-drug resistance associated protein (MRP) following antisense oligodeoxynucleotide (AS-ODN) treatment involving ^{99m}Tc-MIBI. ***Methods:*** The human breast cancer MCF-7 cell line and its MDR-induced MCF-7/VP cell line were employed. Cell suspensions of the two cell lines at 1×10^4 cells/m*l* were inoculated in 24-well plates (0.2 m*l*/well) and incubated for one day. Antisense (AS) 20-mer phosphorothioate ODN complementary to the coding region of MRP mRNA and its sense (S) ODN were administered at final concentrations up to 25 μM, followed by a 5-day incubation. ^{99m}Tc-MIBI solution was added to each well and incubated for 30 min. Cellular ^{99m}Tc-MIBI uptake was corrected for protein concentration. MRP mRNA expression levels were analyzed via the reverse transcription polymerase chain reaction (RT-PCR). ***Results:*** Cellular uptake of ^{99m}Tc-MIBI in MCF-7/VP cells was only 15% of that of MCF-7 cells. Following AS-ODN treatment at 25 μM for five days, ^{99m}Tc-MIBI uptake in MCF-7/VP cells increased 2.4-fold in comparison with non-treated control cells. ^{99m}Tc-MIBI uptake in MCF-7 cells was unaffected by AS-ODN administration. Sense ODN did not alter uptake in either cell line. RT-PCR confirmed reduction of MRP mRNA in MCF-7/VP cells following AS-ODN treatment. ***Conclusion:*** Effects of AS-ODN administration on MRP function can be monitored via assessment of cellular uptake of ^{99m}Tc-MIBI.

Key words: ^{99m}Tc-sestamibi, multi-drug resistance, multi-drug resistance associated protein, antisense, oligodeoxynucleotide