AL08 **Development of type of probes with controlled pharmacokinetics for radiotheranostics aiming integration between diagnosis and therapy**

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Originally, “theranostics” is a coined word between therapeutics and diagnostics. In recent years, it has attracted attention as safe and effective medicine by fusion of diagnosis and therapy. To establish the theranostics system, radiotheranostics using radiolabeled probes is considered to be effective.

Biological functions can be imaged and determined by Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT) with radiolabeled probes in nuclear medicine. There are not only radioisotopes, which emit radiation for diagnosis (gamma rays with high permeability), but also radioisotopes, which emit radiation for therapy (α particles or β^- particles with high cell killing ability). There are also diagnostic and therapeutic radioisotopes with similar chemical properties. Probes for radiotheranostics aiming for integration of diagnosis and therapy are efficiently developed by introducing the diagnostic and therapeutic radioisotopes into same precursor. Since the diagnostic and therapeutic probes are expected to show nearly equal pharmacokinetics, the absorbed radiation doses derived from a therapeutic probe, namely therapeutic effects and side effects, are predictable using imaging data obtained by PET or SPECT imaging analysis after administration of a diagnostic probe. Accordingly, radiotheranostics makes selection of patients and optimization of doses for appropriate therapy possible. That is to say, it can realize personalized medicine.

I have developed probes for radiotheranostics by a molecular design concept combining “target recognition unit”, “radioisotope binding unit”, and “linker unit”. Probes for metastatic bone cancer were developed by combination between bisphosphonate for a carrier to bone cancer as “target recognition unit” and ligands for stable complexes with ^{99m}Tc and ^{68}Ga, which are easily available at the clinical site by the generator system, as “radioisotope binding unit” via “linker unit”. Namely, MAG3, which forms stable complexes with ^{99m}Tc and $^{186/188}$Re, conjugated bisphosphonate and DOTA, which forms stable complexes with ^{68}Ga, ^{90}Y, and ^{177}Lu, conjugated bisphosphonate were designed and synthesized. $^{186/188}$Re, ^{90}Y, and ^{177}Lu have been used as therapeutic radioisotopes. ^{99m}Tc-MAG3 conjugated bisphosphonate and ^{67}Ga-DOTA conjugated bisphosphonate showed excellent biodistribution comparable to that of ^{99m}Tc-HMDP, which has been used in clinical. The results mean usefulness of the probes and validity of the drug design. Next, ^{186}Re-MAG3 conjugated bisphosphonate and ^{90}Y-DOTA conjugated bisphosphonate as the corresponding therapeutic probes were synthesized and evaluated. The validity of the research strategy was demonstrated.

Vesamicol with high affinity for sigma-1 receptor was used as a lead compound and probes labeled with radiohalogens were synthesized and evaluated to develop for sigma-1 receptor targeting probes for diagnosis and therapy of cancer. Recently, the use of α particles, which can be expected to have high therapeutic effects, has attracted attention. I developed an α -particle emitting radionuclide, ^{211}At, labeled sigma-1 receptor targeting probe, and showed the possibility of the radiotheranostics with α -particle emitting radionuclides.

In this presentation, I will introduce the above-mentioned and some other probes, which were prepared based on the “radiotheranostics” concept, for cancer diagnosis and therapy.