Development of ^{211}At-radiopharmaceuticals for Targeted Alpha Therapy in Cancer

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Targeted alpha therapy (TAT) is a promising targeted treatment for cancer, which employs cancer-targeting molecules labeled with short-lived radionuclides capable of emitting α ray. TAT is known for its ability to provide superior efficacy in eliminating cancer cells due to the high energy of the α particles. TAT also has the benefit of limited invasion to surrounding organs due to the short range of α ray, and negligible radiation leakage from the patient, thus eliminating the need for isolation wards. Of particular interest for us is ^{211}At with a half-life of 7.2 hours. With rapid tumor accumulation, high therapeutic efficacy can be achieved while minimizing side effects. Osaka University has established facilities for the production of ^{211}At using an accelerator, chemical synthesis and preclinical and clinical investigations of ^{211}At drugs. Notably, a physician-led clinical trial for treating refractory thyroid cancer with Na^{211}At was launched in 2021.
Aiming to develop a more broadly applicable ^{211}At drug, We have developed α-methyl-L-tyrosine labeled with ^{211}At (^{211}At-AAMT) as a TAT drug targeting the cancer-specific L-type amino acid transporter 1 (LAT1). ^{211}At-AAMT efficiently inhibited tumor growth in the PANC-1 tumor model mice as well as metastasis in the lung of the B16F10 metastasis model (Figure 1) [1]. We also have developed ^{211}At-labeled PSMA, which effectively suppressed tumor growth in prostate cancer model mice while minimizing harm to healthy organs [2]. Applications of ^{211}At-TAT to biologics such as antibodies will also be reported.

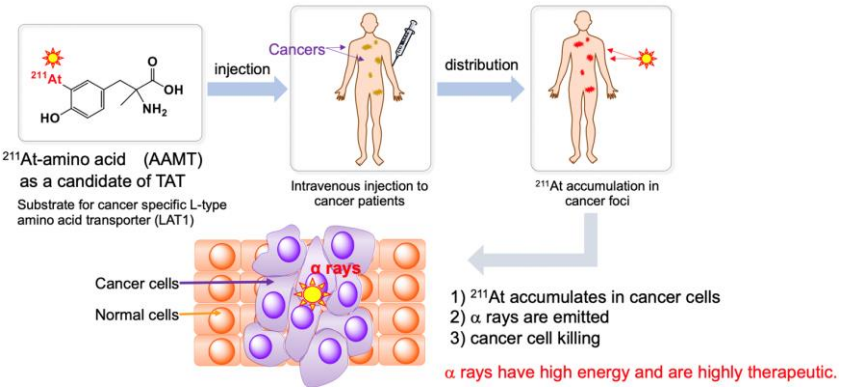

Figure 1. Targeted alpha therapiy.

References

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[2] Watabe, T.; Kaneda-Nakashima, K.; Shirakami, Y.; Kadonaga, Y.; Ooe, K.; Wang, Y.; Haba, H.; Toyoshima, A.; Cardinale, J.; Giesel, F. L.; Tomiyama, N.; Fukase, K. *Eur. J. Nucl. Med. Mol. Imaging* **2023**, *50*, 849-858.