5–3 Clear Imaging of Tumor with D-Amino Acid

— Development of a Novel Amino Acid Tracer, D-[^{18}F]FAMT, for PET Diagnosis of Cancer —

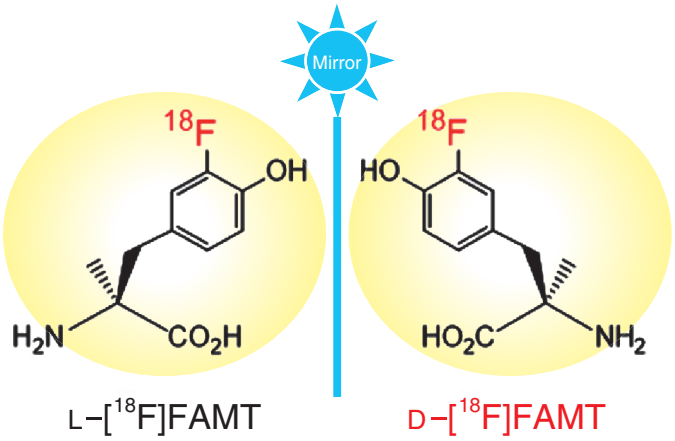

Fig.5-7 Structure of L-[^{18}F]FAMT and D-[^{18}F]FAMT
L-[^{18}F]FAMT (left) and D-[^{18}F]FAMT (right) are enantiomers of each other. Their structures are mirror images of each other, as in the relationship between the left and right hands.

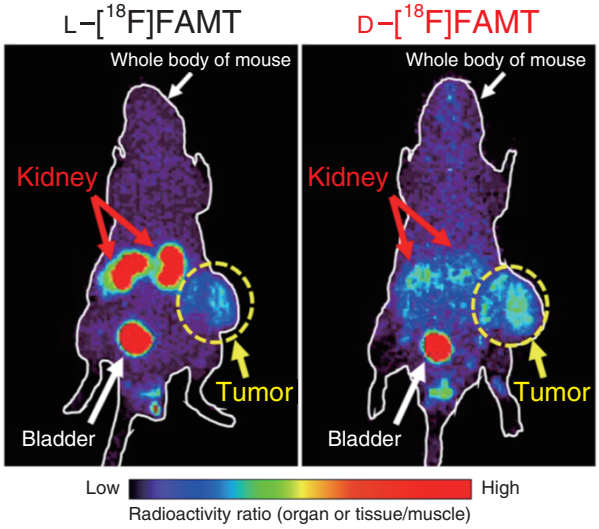

Fig.5-8 Comparison of images with L-[^{18}F]FAMT and D-[^{18}F]FAMT
In the image with L-[^{18}F]FAMT (left), renal accumulation was high and the tumor contrast was low, whereas, in the image with D-[^{18}F]FAMT (right), the renal accumulation was low and the entire tumor was clearly imaged. (The same mouse was used for all PET imaging.)

Diagnosis with positron emission tomography (PET) is a useful tool for understanding the physiological status of cancer, as well as for early detection. In PET diagnosis, γ-rays emitted from the patient are quantitatively detected outside of the body after the injection of PET tracers, and reconstructed images are used for diagnosis. 3-[^{18}F]fluoro-α-methyl-L-tyrosine (L-[^{18}F]FAMT), an amino acid derivative, is clinically used for definitive diagnosis because it is selectively taken up by malignant tumors. However, because L-[^{18}F]FAMT is also accumulated and retained in the kidney and pancreas, it exhibits slow clearance from the blood. Therefore, the border between a malignant tumor and benign tissue in the images is unclear, making it hard to distinguish the region of the tumor accurately. For accurate diagnosis, we aimed to develop a new tracer that enables clear visualization of tumors by improving the non-specific accumulation and retention of L-[^{18}F]FAMT.

The new tracer should have a low affinity to both renal and pancreatic cells. The chemical structure is generally modified to avoid uptake into the cells. However, we thought that accumulation and retention in the kidney and pancreas could be suppressed while retaining the advantage of L-[^{18}F]FAMT, not by modification of the chemical structure, but by using the fact that D-amino acids, the enantiomers of L-amino acids, rarely accumulate in normal tissue and are rapidly excreted from the kidney to urine. Consequently, we developed 3-[^{18}F]fluoro-α-methyl-D-tyrosine (D-[^{18}F]FAMT) (Fig.5-7).

Biodistribution studies in tumor-bearing mice showed that D-[^{18}F]FAMT rapidly cleared from the blood, and less of it accumulated in the kidney and pancreas, compared to L-[^{18}F]FAMT. Although the amount of D-[^{18}F]FAMT in the tumor was reduced, the tumor-to-blood ratio of D-[^{18}F]FAMT was higher than that of L-[^{18}F]FAMT. PET imaging with D-[^{18}F]FAMT showed high tumor-to-background contrast and low accumulation in the kidney, indicating that D-[^{18}F]FAMT could exhibit lower renal accumulation and enable clear visualization of the tumor (Fig.5-8).

If PET using D-[^{18}F]FAMT is widely applied, cancer therapy based on more accurate diagnosis would be expected. Furthermore, D-[^{18}F]FAMT would be an effective tracer for renal and pancreatic cancer, which cannot be detected using L-[^{18}F]FAMT. In the future, we will perform a toxicological analysis of D-[^{18}F]FAMT to support practical application.

Reference

Ohshima, Y. et al., Biological Evaluation of 3-[^{18}F]Fluoro-α-Methyl-D-Tyrosine (D-[^{18}F]FAMT) as a Novel Amino Acid Tracer for Positron Emission Tomography, Annals of Nuclear Medicine, vol.27, no.4, 2013, p.314–324.