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Critical moieties of aromatic amino acid probes causing renal accumulation in tumor imaging

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As molecular probes for cancer diagnosis, [^{18}F]FAMT (3-[^{18}F]fluoro-α-methyl-l-tyrosine) and [^{123}I]IMT (3-[^{123}I]iodo-α-methyl-l-tyrosine) have been used clinically due to their high selectivity to cancer-specific amino acid transporter LAT1 (SLC7A5). However, FAMT and IMT exhibit strong physiological background only in the kidney. Previous study shows FAMT is a substrate of organic ion transporters. Moreover, it has been confirmed that the renal excretion of the probes was inhibited by probenecid, so the organic anion transporter OAT1 (SLC22A6) that mediates urinary excretion of organic anions is supposed to be important for the renal accumulation of the probes. Here, we examined a series of aromatic amino acid derivatives with the altered positions for hydroxyl groups and halogen groups on the aromatic ring. By comparing their IC_{50}s to inhibit the uptake of *para*-aminohippurate by OAT1 and their efflux profiles, we revealed that both halogen and hydroxyl group on the benzene ring of FAMT and IMT are critical for the interaction, whereas the α-methyl moiety essential for the selectivity to LAT1 is not important to interact with OAT1. The results would benefit for the design of the tumor-specific imaging probes with less renal background and the radionuclide therapeutic agents with less adverse renal damage.