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# Transcellular transport of radioiodinated 3-iodo-$\alpha$-methyl-L-tyrosine across monolayers of kidney epithelial cell line LLC-PK$_1$

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***Objective:*** 3-[$^{123}$I]iodo-$\alpha$-methyl-L-tyrosine ([$^{123}$I]IMT) is an imaging agent for amino acid transport. In order to obtain fundamental data related to tumor imaging with [$^{123}$I]IMT and renal physiological accumulation of [$^{123}$I]IMT, we investigated the transport characteristics of [$^{125}$I]IMT in porcine kidney epithelial cell line LLC-PK$_1$ using cell monolayers grown on microporous membrane filters. ***Methods:*** LLC-PK$_1$ monolayers were created on a collagen-coated microporous (3 $\mu$m) membrane (4.7 cm$^2$). To examine transcellular transport (secretion and reabsorption) and accumulation, the monolayers were incubated for up to 90 min at 37°C with 18.5 kBq [$^{125}$I]IMT in Dulbecco's phosphate-buffered saline (pH 7.4) as an uptake solution. After incubation, transcellular transport was assessed by quantifying the radioactivity of the solutions on each side of the monolayer. For the accumulation experiment, the cells were solubilized in NaOH solution, and the radioactivity was quantified. For the inhibition experiment, the inhibitor was added at a final concentration of 1 mM. For the pH dependence experiment, the pH of the apical-side uptake solution was varied from pH 5 to pH 8. Transport of [$^{14}$C]Tyr was examined for comparison. ***Results:*** Bi-directional transcellular transport of [$^{125}$I]IMT was observed, corresponding to secretion and reabsorption in proximal tubule. Accumulation of [$^{125}$I]IMT from the basolateral side (1.62 $\pm$ 0.15%) and the apical side (2.62 $\pm$ 0.35%) was observed at 90 min. 2-Amino-bicyclo[2,2,1]heptane-2-carboxylic acid (a specific inhibitor of system L), L-Tyr (mother compound of [$^{125}$I]IMT) and 2-aminoisobutyric acid (an inhibitor of system L and A) inhibited both directional transport ($p < 0.01$) and accumulation ($p < 0.01$). 2-(Methylamino)isobutyric acid (a specific inhibitor of system A) appeared to inhibit transport and accumulation, but the results were not significant. Decreasing apical pH significantly enhanced accumulation of [$^{125}$I]IMT from both sides ($p < 0.001$), whereas accumulation of mother L-Tyr was significantly suppressed. ***Conclusions:*** The inhibition experiments suggest that the main contributor to [$^{125}$I]IMT transport is system L, rather than $Na^+$-dependent transport, in both apical and basolateral membrane. [$^{125}$I]IMT was transported by the system that transported L-Tyr, but the observed pH dependence of transport suggests that different mechanisms are involved in accumulation of [$^{125}$I]IMT and [$^{14}$C]Tyr.

**Key words:** amino acid transport, system L, epithelial cell line, LLC-PK$_1$, 3-iodo-$\alpha$-methyl-L-tyrosine