Characterization of pre-incubation inhibitory effects of JPH203 on L-type amino acid transporter 1 function.

Kentaro Okunushi^{1,2}, Tomomi Furihata¹, Kosuke Higuchi¹, Yoshie Reien¹, Kiyoshi Nakagawa¹, Naoki Simojo², Naohiko Anzai¹

¹Dept. Pharm., Grad. Sch. Med., Chiba Univ., ²Dept. Pediatrics, Grad. Sch. of Med., Chiba Univ.

BACKGROUND/AIM: JPH203 is a novel anti-cancer drug targeting L-type amino acid transporter 1 (LAT1), which plays a key role in essential amino acid uptake in cancer cells. While the co-incubation inhibitory effect of JPH203 has been characterized in conventional uptake assay, its pre-incubation inhibitory effects remain undetermined. Therefore, we aimed to characterize pre-incubation inhibitory effects of JPH203 on LAT1 function. **METHODS:** Pre-incubation effects were examined by leucine uptake assay using LAT1-positive human colon cancer HT-29 cells. **RESULTS:** In time-dependency analysis, pre-incubation of HT-29 cells with 10 μ M JPH203 for 30, 60, and 120 min resulted in a significant decrease of the leucine uptake activity (42%, 32%, and 28% of those obtained from the control cells, respectively). Similarly, in concentration-dependency analysis, pre-incubation of the cells with JPH203 (1, 10, and 30 μ M for 120 min) decreased the activity level to 68%, 25%, and 3% of those of the control cells, respectively. **CONCLUSION:** We have identified potent pre-incubation inhibitory effects of JPH203 on LAT1 function. Combination effects of pre- and co-incubation inhibitory effects are currently under examination.