Adjusting serum urate level by affecting membrane transporters involved in the disposition of urate

学 位 論 文 概 要

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Adjusting serum urate level by affecting membrane transporters involved in the disposition of urate

(和訳)

輸送体を介した血清尿酸値調節

生命科学 専攻 分子作用学 講座

氏 名 盧 楊

主任指導教員氏名 玉井 郁巳

学位論文概要

This thesis investigates roles of urate-related transporters (e.g. URAT1/SLC22A12, URATv1/SLC2A9, and BCRP/ABCG2) in adjusting serum urate (SUA) level under physiological and disease conditions. In Chapter 2, functional cooperation of sodium-dependent monocarboxylate transporters (SMCTs) and urate transporter 1 (URAT1) was demonstrated indicating that SMCTs indirectly regulates urate reabsorption mediated by URAT1 function; therefore SMCT may serve as a potential target for the alteration of renal urate handling. In Chapter 3, interaction of whisky congeners with urate transporters was studied as a new rationale for their SUA-lowering effect. Since URAT1-mediated urate uptake was significantly inhibited by whisky congeners, it is conceivable that SUA-lowering effect of drinking whisky may be caused by blocking URAT1 by congeners abundantly contained in whisky. In Chapter 4, association of increased uremic toxins with extra-renal elimination of urate mediated by urate efflux transporter, breast cancer resistance protein (BCRP). In patients with chronic kidney disease, although renal function is greatly reduced, SUA level is relatively maintained. Indoxyl sulfate, as a model uremic toxin, induced significantly transport activity of BCRP in Caco-2 cells, such compensatory increase of extra-renal urate excretion may contribute to balance SUA. In conclusion, SUA can be adjusted directly or indirectly by urate transporters, providing their physiological significance in urate homeostasis.