NPT4 is a member of type I sodium-dependent phosphate cotransporter, solute carrier family 17 (SLC17A3). It has recently been reported as voltage-driven organic anion transporter located at apical renal proximal tubule (Jutabha et al. J Biol Chem, 2010). NPT4 functions as an efflux transporter for various organic anionic compounds including para-aminohippurate (PAH) and urate. Using Xenopus oocytes expressing NPT4, [14C]urate transport into oocytes with depolarized condition was inhibited in the presence of various diuretics, including loop diuretics and thiazides, but not carbonic anhydrase inhibitors.

To clarify whether loop diuretics and thiazides are substrates of NPT4, NPT4-injected oocytes were incubated in the solution containing diuretics compare to control oocytes. LC/MS/MS analysis showed that furosemide, bumetanide, hydrochlorothiazide, trichlormethazide and chlorothiazide, but not acetazolamide were significantly transported into oocytes expressing NPT4. Therefore, diuretics-induced hyperuricemia can be explained by the interaction of diuretics on NPT4-mediated urate efflux during the secretion of diuretics across renal proximal tubule.