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The involvement of Na⁺K⁺2Cl⁻ co-transporter in the development of renal chronic failure

Sara Damiano¹, Maria Valeria Puzio¹, Roberto Ciarcia¹, Enrica Zona², Miriam Zaccchia, Giovanna Capolongo², Luigi Avallone¹, Salvatore Florio¹ and Giovambattista Capasso²¹University of Naples Federico II, Italy²Second University of Naples, Italy

Cyclosporine A (CsA) has provided new perspective to prevent organ transplant rejection. However, the use of CsA is limited by several chronic renal diseases, including hypertension. The development of the hypertension is related to sodium and water retention in the kidney, regulated by the sodium transporters along the nephron: the sodium/hydrogen exchanger isoform 3 (NHE3) in the proximal tubule (PT) and the apical sodium two-chloride potassium co-transporter (NKCC2) in the thick ascending limb of the Henle loop (TAL). In this work we have investigated, in a rat animal model and in human transplant patients treated with CsA, the role of the sodium transporters. After the rats were treated for 21 days with CsA, we have measured the renal sodium and water reabsorption in PT and in the TAL by *in vivo* micro-puncture experiments showing a significant reduction of the PT reabsorption and an increase of the NKCC2 in the TAL. The molecular biological data, obtained by Western blot and RT-PCR, have confirmed the micro-puncture data showing a clear increase in NKCC2. In human transplant patient treated with CsA, we investigated the excretion of NKCC2 in the urinary exosomes and we observed a higher amount of NKCC2 than in non-CsA-treated patients. Our results suggested a key role of NKCC2 in the TAL as an important site of sodium retention in cyclosporine-induced hypertension. This data may have potential clinical implications for the treatment of chronic renal diseases like CsA- hypertension.

Biography

Sara Damiano is a Biotechnology-Veterinary graduate and has done her PhD in Nephrology Science. She is specialized in *in vivo* studies of Renal Physiology and Pathophysiology in animal models. Her principal research interests are the studies of hypertension in spontaneously hypertensive animal model and the development of nephrotoxicity induced by immunosuppressive drugs. She has published more than 16 international papers and 2 national papers. She has received a Fellowship for the study and research on Renal Physiology by FROMO; and in 2010 Fellowship for study and research on Renal Physiology by SIN (Italian Society of Nephrology). She is the Principal Investigator in a project STAR 2014.

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