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## Muscle-derived exosome/miR-29 attenuates kidney fibrosis in UUO mice

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We hypothesized that intramuscular injection of exosome encapsulated miR-29 would counteract unilateral ureteral obstruction (UUO)-induced muscle wasting and renal fibrosis via exosome-mediated muscle-kidney crosstalk. Exosomes containing miR-29 (Exo/miR29) were prepared from the satellite cells and injected into the tibialis anterior muscle of UUO mice for one to four weeks. The expression of miR-29 was decreased in skeletal muscle and kidney of UUO mice. Serum from UUO mice enhanced secretion of exosome-encapsulated miR-29 from cultured C2C12 skeletal muscle and HEK293 renal cells. The intervention of Exo/miR29 increased muscle cross-section area and decreased UUO-induced upregulation of TRIM63/MuRF1 and FBXO32/atrogen-1. Curiously, BUN was decreased in the mice treated with Exo/miR29. In addition, renal fibrosis was partially depressed in the UUO mice with intramuscular injection of Exo/miR29. This was confirmed by decreased TGF $\beta$ , alpha-smooth muscle actin ( $\alpha$ SMA), fibronectin, collagen 1A1 and 4A1 in the kidney of UUO mice by muscle-derived miR-29. When we used fluorescence-labeled Exo/miR-29 to trace the Exo/miR route in-vivo we found that fluorescence was significantly visible in both injected and un-injected muscle and in kidneys. The fluorescence intensity in kidney correlated with skeletal muscle. We found that miR-29 directly inhibits TGF- $\beta$ 3 in cultured kidney cells. We conclude that exosomes play a critical role in muscle-kidney crosstalk. Muscle-derived Exo/miR29 not only ameliorates skeletal metabolism, but also attenuates UUO-induced kidney fibrosis by down-regulating TGF- $\beta$  pathway proteins and extracellular matrix components.

### Biography

Zhen Su has completed her MD from Wenzhou Medical University; PhD from Second Military Medical University, and; Post-doctoral studies from Emory University School of Medicine. She is the Vice-Principle Investigator of renal division in the First Affiliated Hospital of Wenzhou Medical University. She has published more than 40 papers in reputed journals and had oral presentation in ASN 2005 (American Society of Nephrology) meeting and WCN 2007 (ISN World Congress of Nephrology) meeting.

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