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### **Therapeutic role of colostrum-derived exosome in chronic kidney disease**

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**Objectives:** Exosome research is being conducted in various fields such as cancer, immune disease, drug delivery, and biomarkers, but research on treatment of kidney disease is insufficient, and exosome isolation and purification technologies still have limitations. Compared to exosomes obtained from cell medium, milk-derived exosomes exhibit high production efficiency, superior stability, biocompatibility, half-life, and very low immunogenicity. Here, the efficacy of milk-derived exosomes in adenine-induced CKD mice were investigated.

**Methods:** The bovine colostrum used in the experiment was collected from cows within 7 days of giving birth to calves. For the mature milk, pasteurized milk was also used, and exosome was extracted from them.

**Results:** First, the protein expression patterns of exosomes extracted from mature milk and bovine colostrum were compared. Colostrum exosomes (Colos-EV) had significantly higher levels of plasminogen, anti-inflammatory factors (clusterin and CD5L protein), cell proliferation and migration factors (lactadherin and IGFBP7 protein), and re-epithelization and angiogenesis factors (apolipoprotein E) compared to mature milk- or serum-derived exosomes, and in vitro study, Colos-EV promoted the tube formation of endothelial cells, whereas serum-derived exosomes had no such effect, suggesting that anti-inflammatory and cell regeneration factors in Colos-EV may be more effective in CKD kidneys. To examine in vivo efficacy of Colos-EV, they were administered to adenine-induced CKD mice twice a week for 4 weeks. Through molecular imaging equipment (IVIS® Lumina), it was confirmed that Colos-EV administered intraperitoneally/intravenously migrated to the kidney more effectively than other organs, and we found that Colos-EV significant improved renal functional deterioration and fibrosis progression in CKD mice.

**Conclusions:** We demonstrated that milk-derived exosomes, especially Colos-EV, have anti-inflammatory and tissue regenerative capacities from proteomic data, and are effective in adenine-induced CKD recovery.