

## 신장 줄기세포 유래 미세입자의 혈관형성 신호 전달 및 신장 보호 작용

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### Microparticles from Kidney Derived-Mesenchymal Stem Cells Act as Carriers of Proangiogenic Signals and Contribute to Renoprotection in Acute Kidney Injury

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**Background:** Microparticles (MP) shed from bone marrow mesenchymal stem cells (MSC) conferred protective effects against acute tubular injury via transfer of messenger RNA and microRNA. We recently demonstrated that in vitro expanded kidney derived-MSC (KMSC, Kidney International 2008; 74:879-889) protected peritubular capillary endothelial cells in acute ischemic reperfusion injury (IRI).

**Methods:** KMSC were cultured in hypoxic chamber in serum deprived MEM with hydrogen peroxide (200 M) for 24 hours. MP were isolated from supernatants by differential ultrafiltration (2,000x g, 10 min, 100,000x g, 1hr) for electron microscopy and flowcytometric characterization and MP RNA was extracted using ExoMir kit (BIO Scientific). Isolated MP were co-cultured with human umbilical vein endothelial cells (HUVEC) on growth factor reduced Matrigel to assess their effect on endothelial tube formation. Mice subjected to bilateral IRI were injected with PKH26 stained MP (4x10<sup>6</sup>/mice) to assess its renoprotective effects.

**Results:** Presence of MP was confirmed by electron microscopy. Flow cytometric analysis of MP demonstrated presence of several adhesion molecules shown to be expressed on KMSC membrane such as CD29, CD44, CD73, alpha4- and alpha 6 integrins. Quantitative real time PCR confirmed the presence of 3 splicing variants of VEGF-A (120, 164, 188) and IGF-1 in isolated MP. MP labeled with PKH26 red fluorescence dye were incorporated by cultured HUVEC via surface molecules such as CD44 and CD29. MP dose dependently improved in vitro HUVEC viability and promoted endothelial tube formation. Furthermore, injection of MP after IRI significantly improved renal function in mice subjected to 32 minutes of bilateral IRI.

**Conclusion:** Our results support the hypothesis that KMSC-derived MP may act as a source of proangiogenic signals and confer renoprotective effects.

**Key Words:** 급성신손상, 줄기세포 유래 미세입자, 혈관형성인자

Acute kidney injury, Microparticle, Proangiogenic factors