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요독증에 의한 골수유래 간엽줄기세포의 기능적 결함

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Uremia Induces Functional Incompetence of Bone Marrow-Derived Stromal Cells

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Background: Chronic kidney disease (CKD) is associated with increased risk for cardiovascular diseases (CVD). We hypothesized that inadequate angiogenic response in uremic patients could result from dysfunction of bone marrow-derived stromal cells (MSCs).

Methods: We investigated whether MSCs are functionally competent in uremia induced by partial kidney ablation in C57Bl/6J mice.

Results: Uremic MSCs showed decreased expression of VEGF, VEGFR1, and stem cell-derived factor (SDF)-1α, increased cellular senescence, decreased proliferation, defects in migration in response to VEGF and SDF-1α, and in vitro tube formation. Interestingly, the expression of fibroblast-specific protein-1 was higher in uremic MSCs. Uremia decreased hypoxia-inducible factor-1α, VEGF, and VEGFR1 expression under hypoxia and Akt phosphorylation in both basal and VEGF-stimulated states. A diminished mitogenic effect on endothelial proliferation was observed in conditioned media from uremic MSCs. In addition, intravital microscopic analysis showed decreased angiogenesis in uremic MSCs.

Conclusion: These results clearly demonstrate the functional incompetence in MSCs under uremic conditions and may significantly contribute to the disproportionately high risk for CVD in patients with CKD.

Key Words: 요독증, 심혈관질환, 골수유래 간엽줄기세포
Uremia, Cardiovascular disease, BM-derived stromal cells