# Paper Five

## Therapeutic potential of mesenchymal stem cells for peripheral artery disease in a rat model of hindlimb ischemia

Mesenchymal stem cells are viewed as the first choice in regenerative medicine. This study aimed to elucidate the influence of BM-MSCs transplantation on angiogenesis in a rat model of unilateral peripheral vascular disease. Materials and Methods: Twenty-one rats were arbitrarily allocated into three groups (7/group). Group I: control sham-operated rats, Group II: control ischemic group: Rats were subjected to unilateral surgical ligation of the femoral artery, and Group III: ischemia group: Rats were induced as in group II, 24 hr after ligation, they were intramuscularly injected with BM-MSCs. After scarification, gastrocnemius muscle gene expression of stromal cell-derived factor-1 (SDF-1), CXC chemokine receptor 4 (CXCR4), vascular endothelial growth factor receptor 2 (VEGFR2), von Willebrand factor (vWF), and hypoxia-inducible factor-1α (HIF-1α) were analyzed by quantitative real-time PCR. Muscle regeneration and angiogenesis evaluation was assessed through H&E staining of the tissue. Furthermore, Pax3 and Pax7 nuclear expression was immunohistochemically assessed. Results: Rats treated with BM-MSCs showed significantly raised gene expression levels of SDF-1, CXCR4, VEGFR2, and vWF compared with control and ischemia groups. H&E staining of the gastrocnemius showed prominent new vessel formation. Granulation tissue within muscles of the ischemic treated group by BM-MSCs showed cells demonstrating nuclear expression of Pax3 and Pax7. Conclusion: BM-MSCs transplantation has an ameliorating effect on muscle ischemia through promoting angiogenesis, detected by normal muscle architecture restoration and new blood vessel formations observed by H&E, confirmed by increased gene expression levels of SDF-1, CXCR4, VEGFR2, and vWF, decreased HIF-1α gene expression, and increased myogenic Pax7 gene expression.