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Micro vesicles secreted by nitric oxide primed mesenchymal stromal cells boost the engraftment potential of hematopoietic stem cells

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Patients with leukemia, lymphoma, severe aplastic anemia, etc. are frequently the targets of bone marrow transplantation, success of which critically depends on efficient engraftment by transplanted hematopoietic cells (HSCs). Early recovery of hematopoiesis is of paramount importance to reduce the post-transplant morbidity and mortality. In autologous settings, HSCs are collected from the patients in remission. These HSCs are already exposed to chemotherapeutic agents, and thus, may possess affected functionality. Similarly, HSCs from older individuals possess compromised engraftment ability due to aging process. Cord blood units yield fewer HSCs, restricting their use to pediatric patients. Ex *vivo* manipulation of HSCs to improve their engraftment ability becomes necessary when the number or quality of donor HSCs is a limiting factor. Due to their hematopoiesis-supportive ability, bone marrow-derived mesenchymal stromal cells (MSCs) have been traditionally used as feeder layers for ex *vivo* expansion of HSCs. MSCs form a special HSC-niche *in vivo*, implying that signaling mechanisms operative in them would affect HSC fate. We have recently demonstrated that AKT signaling prevailing in the MSCs affect the HSC functionality. Here we show that MSCs primed with nitric oxide donors significantly boosts the engraftment potential of the HSCs co-cultured with them via horizontal transfer of mRNAs encoding HSC-supportive genes via microvesicles (MVs). Our data suggest that these MVs could be used as HSC-priming agents to improve transplantation efficacy. Since both, nitric oxide donors and MSCs are already in clinical use; their application in clinical settings may be relatively straight forward. This approach could also be applied in regenerative medicine protocols.

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