

Host preconditioning

Functional decline of stem cell transplantation in ageing hosts is well documented. The mechanism for this is poorly understood, although it is known that advancing age does not provide an optimal milieu for exogenous stem cells to survive, engraft and differentiate.

Lee et al. showed that n-butyldenephthalide improved human adipose-derived stem cell (hADSC) engraftment via attenuating the production of reactive oxygen species (ROS). It remained unclear whether pre-treated hosts with n-butyldenephthalide can rejuvenate the ageing heart and improve hADSC engraftment by regulating the ROS/NLRP3 inflammasome-mediated cardiac fibrosis after myocardial infarction. One hour after coronary ligation, hADSCs were transplanted into the hearts of young and ageing Wistar rats that were pre-treated with or without n-butyldenephthalide for 3 days. At day 3 after infarction, myocardial infarction was associated with an increase in ROS levels and NLRP3 inflammasome activity with age. hADSC transplant effectively provided a significant decrease in ROS levels, NLRP3 inflammasome activity, IL-1 β levels and cardiac fibrosis in either young or old infarcted rats. However, the beneficial effects of hADSCs were greater in young compared with old rats in terms of NLRP3 inflammasome activity. The infarcted ageing rats pre-conditioned by n-butyldenephthalide improved engraftment and differentiation of hADSCs and additionally attenuated cardiac fibrosis compared with hADSCs alone. The anti-inflammation effects of n-butyldenephthalide were reversed by SIN-1. In conclusions, the increased NLRP3 inflammasome activity plays the pathogenesis of ageing-related functional hADSC decline in the ageing hosts. n-butyldenephthalide-pre-treated ageing hosts reversibly ameliorate the harsh microenvironments, improve stem cell engraftment and attenuate cardiac fibrosis after myocardial infarction ¹⁾.

¹⁾

Lee TM, Harn HJ, Chiou TW, Chuang MH, Chen CH, Chuang CH, Lin PC, Lin SZ. Host pre-conditioning improves human adipose-derived stem cell transplantation in ageing rats after myocardial infarction: Role of NLRP3 inflammasome. J Cell Mol Med. 2020 Oct 6. doi: 10.1111/jcmm.15403. Epub ahead of print. PMID: 33022900.

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