Human wharton's jelly-derived mesenchymal stem cells minimally improve the growth kinetics and cardiomyocyte differentiation of aged murine cardiac c-kit cells in in vitro without rejuvenating effect

ABSTRACT

Cardiac c-kit cells show promise in regenerating an injured heart. While heart disease commonly affects elderly patients, it is unclear if autologous cardiac c-kit cells are functionally competent and applicable to these patients. This study characterised cardiac c-kit cells (CCs) from aged mice and studied the effects of human Wharton's Jelly-derived mesenchymal stem cells (MSCs) on the growth kinetics and cardiac differentiation of aged CCs in vitro. CCs were isolated from 4-week- and 18-month-old C57/BL6N mice and were directly co-cultured with MSCs or separated by transwell insert. Clonogenically expanded aged CCs showed comparable telomere length to young CCs. However, these cells showed lower Gata4, Nkx2.5, and Sox2 gene expressions, with changes of 2.4, 3767.0, and 4.9 folds, respectively. Direct co-culture of both cells increased aged CC migration, which repopulated 54.6 ± 4.4% of the gap area as compared to aged CCs with MSCs in transwell (42.9 ± 2.6%) and CCs without MSCs (44.7 ± 2.5%). Both direct and transwell co-culture improved proliferation in aged CCs by 15.0% and 16.4%, respectively, as traced using carboxyfluorescein succinimidyl ester (CFSE) for three days. These data suggest that MSCs can improve the growth kinetics of aged CCs. CCs retaining intact telomere are present in old hearts and could be obtained based on their self-renewing capability. Although these aged CCs with reduced growth kinetics are improved by MSCs via cell–cell contact, the effect is minimal.

Keyword: Aged cardiac c-kit cells; Wharton's jelly-derived mesenchymal stem cells; Co-culture; Cardiomyocyte differentiation