Impaired redox environment modulates cardiogenic and ion-channel gene expression in cardiac-resident and non-resident mesenchymal stem cells

ABSTRACT

Redox homeostasis plays a crucial role in the regulation of self-renewal and differentiation of stem cells. However, the behavioral actions of mesenchymal stem cells in redox imbalance state remain elusive. In the present study, the effect of redox imbalance that was induced by either hydrogen peroxide (H_2O_2) or ascorbic acid on human cardiac-resident (hC-MSCs) and non-resident (umbilical cord) mesenchymal stem cells (hUC-MSCs) was evaluated. Both cells were sensitive and responsive when exposed to either H_2O_2 or ascorbic acid at a concentration of 400 µmol/L. Ascorbic acid pre-treated cells remarkably ameliorated the reactive oxygen species level when treated with H_2O_2. The endogenous antioxidative enzyme gene (Sod1, Sod2, TRXR1 and Gpx1) expressions were escalated in both MSCs in response to reactive oxygen species elevation. In contrast, ascorbic acid pre-treated hUC-MSCs attenuated considerable anti-oxidative gene (TRXR1 and Gpx1) expressions, but not the hC-MSCs. Similarly, the cardiogenic gene (Nkx 2.5, Gata4, Mlc2a and β-MHC) and ion-channel gene (I_{KDR}, I_{KCa}, I_{to} *and* $I_{Na.TTX}$) expressions were significantly increased in both MSCs on the oxidative state. On the contrary, reduced environment could not alter the ion-channel gene expression and negatively regulated the cardiogenic gene expressions except for troponin-1 in both cells. In conclusion, redox imbalance potently alters the cardiac-resident and non-resident MSCs stemness, cardiogenic, and ion-channel gene expressions. In comparison with cardiac-resident MSC, non-resident umbilical cord-MSC has great potential to tolerate the redox imbalance and positively respond to cardiac regeneration.

Keyword: Human umbilical cord mesenchymal stem cell; Human cardiac mesenchymal stem cell; Oxidative stress; Redox balance; Cardiac gene expression; Ion-channel gene expression