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POSTER ABSTRACTS

711.CELL COLLECTION AND PROCESSING

Diverse Effects of Cryopreservation-Induced Mitochondrial Dysregulation on Cord Blood Cells

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Umbilical cord blood transplantation (UCBT) has been performed broadly in clinic by the specific biological and immunological characteristics of umbilical cord blood cells (UCB). UCB-based cell therapy and immune therapy also presents great application potential. UCB was usually cryopreserved for several years before using. Whether and how cryopreservation affects the function of divergent cell populations in UCB still remain to be illuminated.
Here, we firstly constructed a single-cell transcriptomic profile of Lineage $^{-}$ CD34 $^{+}$ hematopoietic stem and progenitor cells (HSPCs) and mononuclear cells (MNCs) collected from fresh and cryopreserved UCB with 1, 5, 10 and 19 years. Subpopulations characterized by higher mitochondrial gene expression (Mito ^{high}) were identified in all cell populations and found to be increased during cryopreservation. Compared with the fresh group, HSC/MPP cells after cryopreservation showed more active cell cycle and lower expression of HSC/MPP signature genes, especially in the Mito ^{high} HSC/MPP cells. Consistently, colony-forming ability as well as long-term hematopoietic reconstitution of HSPCs derived from cryopreserved UCB gradually decreased within 5 years but remained stable thereafter. More importantly, we observed decreased megakaryocyte differentiation ability from cryopreserved HSPCs, which could be partially rescued by antioxidants treatment after cryopreservation. Mechanically, we revealed that the metabolic dysregulation of mitochondria including elevated mitochondrial reactive oxygen species (ROS), reduced adenosine triphosphate (ATP) synthesis and impaired mitochondrial membrane potential of cryopreserved HSPCs led to attenuated hematopoietic reconstitution. Although there was a mild increase of Mito ^{high} subpopulations after cryopreservation, the cytokine production levels of T cells and NK cells were comparable to those of fresh samples. Additionally, NK cells exhibited almost same cytotoxic function with the fresh compartments.
Taken together, we elucidated the impact of cryopreservation on UCB HSPCs and provided the strategy for rescuing itsfunctional impairment. The unaffected T and NK cells after cryopreservation also paved the way for UCB-based cell therapy and immune therapy. Our study provides important implements for the quality control of applicable UCB both in hematology and immunotherapy.

Disclosures No relevant conflicts of interest to declare.

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