Göteborg, 2017

Exploring the heterogeneity of the hematopoietic stem and progenitor cell pool in cord blood

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs Universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3 Göteborg, tisdagen den 14 november 2017, kl. 9.00 av

Sofia Frändberg, Leg. läkare

Fakultetsopponent:

Professor Ramin Lotfi

Institutionen för Transfusionsmedicin, Ulms Universitet, Tyskland

Avhandlingen baseras på följande delarbeten:

I. **High quality cord blood banking is feasible with delayed clamping practices. The eight-year experience and current status of the national Swedish Cord Blood Bank**.
Frändberg S, Waldner B, Konar J, Rydberg L, Fasth A, Holgersson J.
Cell Tissue Bank. 2016 Sep; 17(3):439-48

II. **Exploring the heterogeneity of the hematopoietic stem and progenitor cell pool in cord blood: simultaneous staining for side population, aldehyde dehydrogenase activity, and CD34 expression.**
Frändberg S, Boreström C, Li S, Fogelstrand L, Palmqvist L.
Transfusion. 2015 Jun; 55(6):1283-9

III. **The aldehyde dehydrogenase cord potency assay excludes early apoptotic cells.**
Frändberg S, Li S, Boreström C, Holgersson J, Palmqvist L,
Submitted

IV. **Concentration of the CDCP1 protein in human cord plasma may serve as a predictor of hematopoietic stem and progenitor cell content.**
Frändberg S, Asp J, Waldner B, Holgersson J, Palmqvist L,
Submitted

SAHLGRENSKA AKADEMIN

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Exploring the heterogeneity of the hematopoietic stem and progenitor cell pool in cord blood

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Abstract

Hematopoietic stem cell transplantation (HSCT) is a curative treatment for a wide range of malignant and hereditary disorders. It is yet the only clinically established stem cell treatment. Hematopoietic stem and progenitor cells (HSPC) can be harvested from bone marrow (BM), stimulated peripheral blood (PBSC) or umbilical cord blood (CB) collected from the placenta after clamping of the cord. A critical factor for the success of HSCT is the dose of functioning HSPC the recipient receives. The National Swedish Cord Blood Bank (NSCBB) was founded in 2005. We compiled the achievements of the NSCBB and investigated the impact of a change of practices from early to delayed clamping on CB collection volume and nucleated cell number. We developed novel methods using flow cytometry for measurement of functional HSPC in CB, firstly for the simultaneous definition of the Hoechst Side Population (SP), Aldehyde Dehydrogenase activity (ALDH) and the expression of the surface protein CD34 and secondly for the definition of viable and apoptotic cells in the ALDH and CD34 positive populations respectively. Finally, we screened for biomarkers in CB plasma that may predict the HSPC content in the corresponding CB collection using a multiplex immunoassay. The NSCBB stands up well in international comparison and the implementation of delayed clamping had no major effect on collection efficiency. There was no overlap between the SP and the ALDH populations, suggesting that they define HSPC pools with different properties. Few apoptotic cells were identified in the ALDH population compared to the viable CD34 positive population, indicating that the ALDH assay intrinsically excludes apoptotic cells. We identified the CDCP-1 protein as a possible biomarker for HSPC content in CB.

Keywords: Cord blood, Cord blood bank, Cord clamping, Hematopoietic stem cell transplantation, Hematopoietic stem and progenitor cells, CD34, Side Population, Aldehyde Dehydrogenase, Apoptosis, CDCP1

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