Identifying transcriptional regulatory mechanisms on stem cells using large scale gene expression profiling.

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Abstract

Hematopoietic stem cells (HSC) are defined by their potential to differentiate into all blood cell lineages as well as by their self renewal potential. In the adult, HSC can be identified in the bone marrow (BM) in a very small population, defined by the expression of the surface protein CD34 in their membrane. Among CD34 positive HSC, the marker CD133 defines an even more primitive subpopulation. In addition to the BM, HSC can be obtained from umbilical cord blood (UCB), a more primitive source, compared to BM. In this lecture we will present our latest progress toward understanding the molecular basis of these intrinsic functional differences, trough the use of gene expression profiling techniques. First we will show how we used Serial Analysis of Gene Expression (SAGE), coupled to promoter analysis of differentially expressed transcripts, to highlight the nuclear factor kappa B (NF-kB) pathway as a distinctive feature of umbilical cord blood (UCB) CD34+ HSC [1]. Then, we will show how we used microarray and correlation analysis of real time quantitative PCR data to point out the potential existence of a highly interconnected transcriptional network, related to the more primitive characteristics of CD133+ (in press). Finally, we show the current efforts in our institution to explore stem cells with a systems biology perspective, with the integration of microarray technologies to evaluate mRNA and microRNA levels.

References

[1] Panepucci, R. A., Calado, R. T., Rocha, V., Proto-Siqueira, R., Silva, W. A., Jr. & Zago, M. A. Higher expression of transcription targets and components of the nuclear factor-kappaB pathway is a distinctive feature of umbilical cord blood CD34+ precursors. Stem Cells. 2007, 25: 189-196.