CD44 Mediates Shear Stress Induced Rolling of Hematopoietic Progenitor Cells and Leukemic Cells on Hyaluronan

CD44 vermittelt scherstrom-induziertes Rolling von hämatopoetischen Vorläuferzellen und leukämischen Zellen auf Hyaluronsäure

Isabel Hoffmann[1], Maximilian Hanke[1,2,3,4], Van T. Hoang[1], Patrick Wuchter[1], Axel Rosenhahn[1,3] and Anthony Ho[4]

1: Department of Medicine V, Heidelberg University, Heidelberg, Germany
2: Institute of Functional Interfaces, Karlsruhe Institute of Technology, Karlsruhe, Germany
3: Applied Physical Chemistry, Heidelberg University, Heidelberg, Germany
4: Analytical Chemistry – Biointerfaces, University of Bochum, Bochum, Germany

Introduction

Recently we could demonstrate the flow induced adhesion and rolling of CD44 expressing hematopoietic progenitor cells (HPC) from umbilical cord blood and of different leukemic cell lines. In this study we examined the expression of different CD44 isoforms in KG-1a, HPC from different sources and leukemic blasts and the specific interaction of these cells with hyaluronic acid (HA) under physiological flow conditions.

Methods

Fresh umbilical Cord Blood (CB), Bone marrow from healthy donors (healthy BM), Peripheral Blood from healthy donors (PB) or G-CSF mobilized peripheral blood from healthy donors (mPB) as well as Bone marrow from patients with newly diagnosed AML (BM AML) were used to isolate $CD34^+$ cells and leukemic blasts. On these cells the expression levels of different CD44 variant isoforms were measured by using flow cytometry. A custom built microfluidic setup was used to apply a defined shear stress for detailed analysis of the interaction of the isolated cells with artificial HA surfaces.

Results

Overall a high CD44pan surface expression could be detected in all tested cell types in contrast to a low CD44variant isoform surface expression. Furthermore, it could be demonstrated that flow induced interaction with HA could be observed for all CD34+ cells from CB, mPB and BM. We could verify that the flow induced rolling on HA was solely CD44 mediated by using a monoclonal anti-CD44 antibody (clone BU52). Additionally to flow induced rolling, we identified an immobile adherence to HA and demonstrated that these two forms of interaction with HA are of different importance in varying sample materials. The immobile adherence was found very pronounced in leukemic blasts from some samples, which in general showed very complex interaction patterns, while it was hardly observed in KG-1a or healthy $CD34^+$ HPC.

Conclusions

We could demonstrate a CD44 mediated, flow induced rolling of KG-1a, HPC, and in parts of leukemic blasts on HA. The interaction of leukemic blasts from patients with AML with HA was highly heterogeneous, in contrast to HPC from healthy materials.