Abstract

CD38 Expression Regulates NAD(H) Levels in Human Leukemia Cells

Introduction: CD38 is a multifunctional protein that is able to act as an ecto NAD(P)ase on a wide variety of cell types. Its expression is also negatively correlated with prognosis in patients with B-CLL. While much is known about its receptorial functions in B-CLL pathogenesis, it is not clear whether the enzymatic functions of CD38 play any role in the process.

Methods: We have used the differentiation of the HL-60 cell line as a model for CD38 expression. HL-60 cells were induced to differentiate via the addition of ATRA (1 μM) for 5 days. NAD(H) was measured by an enzymatic cycling assay, CD38 expression by qPCR and CD38 activity was measured using fluorescent NGD assay.

Results: We have measured the consequences of CD38 expression during the differentiation on a number of functions linked to NAD(P). CD38 expression increases significantly after stimulation with all-trans retinoic acid (ATRA) over the first 24 hours and then remains high throughout 5 days of treatment. This expression pattern correlates well with a drop in intracellular NAD levels of c.50% that could be inhibited with the CD38 inhibitor kuromanin. Surprisingly, the NAD^+/NADH ratio did not change appreciably, but several NAD-dependent processes (glycolysis, antioxidant status, oxidative damage) were found to be significantly affected by the lowered NAD levels.

Conclusion: These data will allow us to investigate whether such changes in NAD(P) levels induced by increased CD38 expression have any clinical significance for the poor prognosis of B-CLL patients expressing high levels of CD38.

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