Ecto-5'-Nucleotidase/CD73 Knockdown Increases Cell Adhesion, Migration and mRNA Level of Collagen I in Hepatic Stellate Cells

Andrade, C. M. B. [1], Lopez, P. L. C. [2], Noronha, B. T. [1], Wink, M. R. [3], Borojevic, R. [4], Margis, R. [1], Lenz, G. [2], Battastini, A. M. O. [1], Guma, F. C. R. [1]
[1]Departamento de Bioquímica, UFRGS. Porto Alegre, RS, Brazil
[2]Departamento de Biofísica, UFRGS, Porto Alegre, RS, Brazil
[3]Departamento de Fisiologia, UFCSPA. Porto Alegre, RS, Brazil
[4]Departamento de Histologia e Embriologia, UFRJ, Rio de Janeiro, RJ, Brazil.

Ecto-5'-nucleotidase (eNT/CD73, E.C.3.1.3.5) is a glycosyl phosphatidylinositol (GPI)-linked cell surface protein with several functions, including local generation of adenosine with consequent activation of adenosine receptors and salvaging of extracellular nucleotides as well as functions apparently independent of its activity, such as mediating cell-cell adhesion. Liver fibrosis may be considered as a dynamic and integrated cellular response to chronic liver injury and the activation of hepatic stellate cells (HSCs) plays a role in the fibrogenic process. Ecto-5'-nucleotidase and adenosine were reported to play an important role in hepatic fibrosis in murine models. To analyze the biological significance of eNT/CD73 in HSC, here we show that eNTC/D73 knockdown leads to an increase in mRNA expression of tissue non-specific alkaline phosphatase (TNALP), another AMP degrading enzyme. eNT/CD73 knockdown also leads to changes in the expression of collagen I and a clear alteration of cell adhesion and migration, despite not altering total ecto-AMPase activity of the cell. We suggest that eNT/CD73 protein expression may control migration by affecting cell-substrate adhesion and collagen expression, in a mechanism not dependent of changes in nucleotide metabolism.

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