The Role of Syndecan-4 in Cellular Behavior

Jarrouge-Bouças,T.R.[1]; Cavalheiro,R.P.[1]; Bouças,R.I.[1]; Trindade,E.S.[2]; Paredes-Gamero,E.J[1]; Dreyfuss,J.L.[1]; Lopes,C.C.[3]; Nader,H.B.[1]

[1]Disciplina de Biologia Molecular, UNIFESP; [2]Departamento de Biologia Celular, UFPR; [3]Departamento de Ciências Biológicas, UNIFESP - Campus Diadema

Heparan sulfate (HS) plays an important role in cell behavior due to its ability to interact with a variety of molecules modulating growth factors and enzymes. HS participates in cellular signaling, and the activation of downstream pathways is related to phosphorylation of cytosolic proteins leading to gene regulation. Syndecan-4 (Syn4) modulates cell adhesion and is involved in the regulation of cell cycle. Recently our laboratory has shown that over-expression of the EJ-ras oncogene in endothelial cells (EJ-ras-EC) alters the cell cycle and up-regulates the expression of Syn4. Syn4 siRNA in endothelial cells (EC) was performed to evaluate the role of Syn4 in these processes. The aim is to establish the role of Syn4 in endothelial cell cycle, adhesion, proliferation, regarding morphologic and molecular alterations. Clones were selected through sqPCR for Syn4 and ^{35}[S]-incorporation into HS. Comparative study using wild type EC, EJ-ras-EC and EC-siRNA-Syn4 was performed to evaluated cell cycle, cellular adhesion and expression of growth factors. Hematoxilin-eosin staining and scanning electron microscopy showed morphologic alterations when comparing the different ECs. EJ-ras-EC showed an increase in the ratio nucleus/cytoplasm, EC-siRNA-Syn4 showed a disorganized cellular arrangement and alteration in filopodia extrusion. Taking into consideration the expression VEGF, RAS, FAK and Syn4, immunofluorescence confocal microscopy confirmed by flow cytometry analyses displayed a up-regulation in EJ-ras-EC and a down-regulation in EC-siRNA-Syn4 for these molecules respectively. Regarding cell proliferation, EJ-ras-EC exhibited a greater incorporation of BrdU when compared to EC, and EC-siRNA-Syn4 a lower incorporation compared to EC. Therefore, the absence of Syn4 leads to alterations in cell cycle and distinct focal adhesion sites, as well as lower levels of VEGF. (CNPq,FAPESP,CAPES). **Key words:** Syndecan-4, endothelial cell, cellular behavior.