

---

## Mesenchymal Stromal Cells Regulate Sialylations of N-Glycans, Affecting Cell Migration and Survival.

|                          |   |
|--------------------------|---|
| <b>Journal:</b>          | Int J Mol Sci   |
| <b>Publication Year:</b> | 2021  |
| <b>Authors:</b>          | Kayla Templeton, Meiby Ramos, Jacqueline Rose, Bryan Le, Qingwen Zhou, Amin Cressman, Stephanie Ferreyra, Carlito B Lebrilla, Fernando Antonio Fierro |
| <b>PubMed link:</b>      | 34206740  |
| <b>Funding Grants:</b>   | CIRM 2.0 Bridges Training Program   |

### Public Summary:

N-Glycosylations are an important post-translational modification of proteins that can significantly impact cell function. Terminal sialic acid in hybrid or complex N-glycans has been shown to be relevant in various types of cancer, but its role in non-malignant cells remains poorly understood. We have previously shown that the motility of human bone marrow derived mesenchymal stromal cells (MSCs) can be modified by altering N-glycoforms. The goal of this study was to determine the role of sialylated N-glycans in MSCs. Here, we show that IFN-gamma or exposure to culture media low in fetal bovine serum (FBS) increases sialylated N-glycans, while PDGF-BB reduces them. These stimuli alter mRNA levels of sialyltransferases such as ST3Gal1, ST6Gal1, or ST3Gal4, suggesting that sialylation of N-glycans is regulated by transcriptional control of sialyltransferases. We next show that 2,4,7,8,9-pentaacetyl-3F-Neu5Ac-CO<sub>2</sub>Me (3F-Neu5Ac) effectively inhibits sialylations in MSCs. Supplementation with 3F-Neu5Ac increases adhesion and migration of MSCs, as assessed by both videomicroscopy and wound/scratch assays. Interestingly, pre-treatment with 3F-Neu5Ac also increases the survival of MSCs in an in vitro ischemia model. We also show that pre-treatment or continuous treatment with 3F-Neu5Ac inhibits both osteogenic and adipogenic differentiation of MSCs. Finally, secretion of key trophic factors by MSCs is variably affected upon exposure to 3F-Neu5Ac. Altogether, our experiments suggest that sialylation of N-glycans is tightly regulated in response to environmental cues and that glycoengineering MSCs to reduce sialylated N-glycans could be beneficial to increase both cell migration and survival, which may positively impact the therapeutic potential of the cells.

### Scientific Abstract:

N-Glycosylations are an important post-translational modification of proteins that can significantly impact cell function. Terminal sialic acid in hybrid or complex N-glycans has been shown to be relevant in various types of cancer, but its role in non-malignant cells remains poorly understood. We have previously shown that the motility of human bone marrow derived mesenchymal stromal cells (MSCs) can be modified by altering N-glycoforms. The goal of this study was to determine the role of sialylated N-glycans in MSCs. Here, we show that IFN-gamma or exposure to culture media low in fetal bovine serum (FBS) increases sialylated N-glycans, while PDGF-BB reduces them. These stimuli alter mRNA levels of sialyltransferases such as ST3Gal1, ST6Gal1, or ST3Gal4, suggesting that sialylation of N-glycans is regulated by transcriptional control of sialyltransferases. We next show that 2,4,7,8,9-pentaacetyl-3F-Neu5Ac-CO<sub>2</sub>Me (3F-Neu5Ac) effectively inhibits sialylations in MSCs. Supplementation with 3F-Neu5Ac increases adhesion and migration of MSCs, as assessed by both videomicroscopy and wound/scratch assays. Interestingly, pre-treatment with 3F-Neu5Ac also increases the survival of MSCs in an in vitro ischemia model. We also show that pre-treatment or continuous treatment with 3F-Neu5Ac inhibits both osteogenic and adipogenic differentiation of MSCs. Finally, secretion of key trophic factors by MSCs is variably affected upon exposure to 3F-Neu5Ac. Altogether, our experiments suggest that sialylation of N-glycans is tightly regulated in response to environmental cues and that glycoengineering MSCs to reduce sialylated N-glycans could be beneficial to increase both cell migration and survival, which may positively impact the therapeutic potential of the cells.