Synopsis of Original Research Paper

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The disruption of communication between epidermal stem cells and their surrounding microenvironment, including adjacent cells and their extracellular matrix (ECM), contributes to the cellular and molecular impairments associated with skin aging. Glycans modify plasma membrane proteins post-translationally and have a role in tissue homeostasis and diseases by regulating cell-cell interactions, ligand-receptor binding, and ECM function. Glycans also play a crucial role in regulating stem cells by modulating signaling pathways that control their self-renewal and differentiation. Our previous study demonstrated age-related alterations in glycosylation patterns in mouse skin, characterized by an upregulation of sialic acid and a downregulation of mannose in aged epidermal stem cells. However, the functional importance of these alterations of glycans in vivo remains still unknown. In this study, we aim to investigate the function of glycosylation in skin aging at the stem cell level. We show that the elevation of a-2,6 sialylation by overexpressing glycogenes (St6gal1 and Man1a) in vivo exhibits phenotypes associated with skin aging, including hair loss, epidermal thinning, and decreased proliferative capacity of epidermal stem cells. Mass spectrometry, using membrane proteins pulled down by lectin probes, identified several potential core protein candidates modified by a-2,6 sialic acid. These findings indicate that changes in glycosylation regulate epidermal stem cell aging by modifying the membrane proteins. The functional relationship between glycogenes and core proteins in regulating epidermal stem cell function is being further investigated, which may provide a molecular basis and a biomarker for skin aging.