Wnt signaling stimulates ATGL-regulated lipolysis in dermal fibrosis

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Wnt signaling stimulates ATGL-regulated lipolysis in dermal fibrosis. Dermal Wnt activation leads to elevated phosphorylated hormone sensitive lipolysis axis is activated in DWAT adipocytes during the onset and progression of Wnt-depletion. Using a genetically inducible and reversible mouse model of dermal Wnt signaling activation stimulates ATGL-regulated lipolysis leading to fibrotic lipid loss. Dermal Wnt signaling is dysregulated in human fibrosis and has known anti-adipogenic roles. We hypothesize that Wnt signaling activation stimulates ATGL-regulated lipolysis leading to fibrotic fat loss in DWAT and the impact of lipid depletion in fibrosis are unknown. Wnt signaling is adipose triglyceride lipase (ATGL)-regulated lipolysis. The mechanisms underlying fibrotic fat loss in DWAT and the impact of lipid depletion in fibrosis are unknown. Wnt signaling is adipose triglyceride lipase (ATGL)-regulated lipolysis. ATLGL enzymatic inhibition is sufficient to rescue Wnt-cell-autonomous lipolytic effects. ATLGL enzymatic inhibition is sufficient to rescue Wnt-induced lipolysis. Current studies focus on the role of ATLGL in Wnt-induced dermal fibrosis in vivo. Our results implicate lipolysis as a novel therapeutic target for fibrosis treatment.

CO-Detection by indexing (CODEX) reveals clinically distinct classes of eczematous rashes

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Spongiotic rashes are known to be more heterogeneous than psoriasiform rashes, but a more precise molecular classification has yet to be established. We performed CO-Detection by indexing (CODEX), which utilizes DNA-barcoded antibodies visualized by cyclic addition and removal of fluorescently labeled complementary DNA oligos, to perform highly multiplexed immunofluorescence on 12 samples of histopathologically spongiotic dermatitis, ranging from allergic contact dermatitis to endogenous eczema. This type of systems-level approach utilizing highly multiplexed spatial imaging, which captures many antigens on a single cell basis, has not been previously utilized in spongiotic dermatitis, nor in any other rashes. We utilized a customized 40 antibody panel allowing enumeration of key APC and T cell types while ascertaining immune cell functional states/signaling status and spatial orientation to skin anatomic structures and cell types. We identified recurrently aberrant immune cell subpopulations enabling subclassification of these rashes into distinct classes correlating with etiology and anatomic site (p < .007). Our findings point to a broadly applicable technology capable of stratifying histopathologically indistinct rashes.