

Epigenetics Regulation Play Role in the Pathogenesis of Adipose Tissue Disorder, Lipedema

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Abstract : Lipedema, a poorly understood chronic disease of adipose hyper-deposition, is often mistaken for obesity and causes significant impairment to mobility and quality-of-life. To identify molecular mechanisms underpinning lipedema, we employed comprehensive omics-based comparative analyses of whole tissue, adipocyte precursors (adipose-derived stem cells (ADSCs)), and adipocytes from patients with or without lipedema. Transcriptional profiling revealed significant differences in lipedema tissue, adipocytes, and ADSCs, with altered levels of mRNAs involved in proliferation and cell adhesion. One highly up-regulated gene in lipedema adipose tissue, adipocytes and ADSCs, ZIC4, encodes Zinc Finger Protein ZIC 4, a class of transcription factor which may be involved in regulating metabolism and adipogenesis. ZIC4 inhibition impaired the adipogenesis of ADSCs into mature adipocytes. Epigenetic regulation study revealed overexpression of ZIC4 is involved in decreased promoter DNA methylation and subsequent decrease in adipogenesis. These epigenetic modifications can alter adipocytes microenvironment and adipocytes differentiation. Our study show that epigenetic events regulate the ability of ADSCs to commit and differentiate into mature adipocytes by modulating ZIC4.

Keywords : lipedema, adipose-derived stem cells, adipose tissue, adipocytes, zinc finger protein, epigenetic

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